

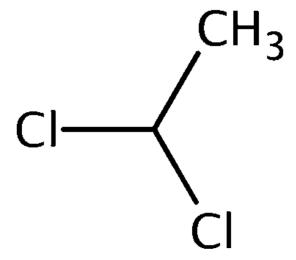
July 2024 Office of Chemical Safety and Pollution Prevention

# Draft Risk Evaluation for 1,1-Dichloroethane

# **Systematic Review Supplemental File:**

Data Quality Evaluation Information for Human Health Hazard Animal Toxicology

CASRN: 75-34-3



This supplemental file contains information regarding the data quality evaluation results for data sources that met the PECO screening criteria for the *Draft Risk Evaluation for 1,1-Dichloroethane* and were used to characterize human health hazard. EPA conducted data quality evaluation based on author-reported descriptions and results; additional analyses (*e.g.*, statistical analyses performed during data integration into the risk evaluation) potentially conducted by EPA are not contained in this supplemental file. EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (also referred to as '2021 Draft Systematic Review Protocol'). Any updated steps in the systematic review process since the publication of the 2021 Draft Systematic Review Protocol are described in *Draft Risk Evaluation for 1,1-Dichloroethane - Systematic Review Protocol*. Within the contents of this document, 1,1-dichloroethane may be referred to as the acronyms 1,1-DCA and 1,1-DCE. The acronyms 1,2-DCE, and DCE refer to the chemical 1,2-dichloroethane. The acronyms 1,1,2-TCE, 1,1,2-TCA, and TCE refer to the chemical 1,1,2-trichloroethane. The acronym trans-1,2-DCE refers to the chemical 1,2-dichloropropane.

1,1-Dichloroethane Table of Contents

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HERO ID Reference Page 1,1-Dichloroethane Acute (less than or equal to 24 hr) 1973137 Dow Chemical, (1947). Results of range-finding toxicological studies on Ethylidene Dichloride. 11 200479 Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro 13 assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530. 644914 Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity 19 studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. 64411 Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicol-23 ogy and Applied Pharmacology 7(1):37-44. Short-term (>1-30 days) 644914 Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity 27 studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. 64411 Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicol-43 ogy and Applied Pharmacology 7(1):37-44. 62395 Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl 45 ethyl ketone in rats. Toxicology and Applied Pharmacology 28(3):452-464. Subchronic (>30-91 days) 1937626 Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. 200479 Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro 50 assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530. 644914 Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity 56 studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. 646679 NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 70 66(1978):1-107. Chronic (>91 days) 1937626 Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-77 265.

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200427	Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice. Environmental Health Perspectives 69:89-95.	110
1973131	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.	122
646679	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.	139
Reproductive/Developmental		
62395	Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in rats. Toxicology and Applied Pharmacology 28(3):452-464.	175
Not reported		
1973137	Dow Chemical, (1947). Results of range-finding toxicological studies on Ethylidene Dichloride.	184
Isomer: Dichloroe	thane	
Acute (less than or equal to 24 h	r)	
5441424	Natsyuk, M. V., Chekman, I. S. (1975). Content of nicotinamide coenzymes in liver and myocardium of rats poisoned with dichloroethane. Bulletin of Experimental Biology and Medicine 79(4):408-409.	186
5441056	Natsyuk, M.V., Fedurov, V.V. (1974). Effect of methyluracil on oxidative phosphorylation in the hepatic mitochondria of rats poisoned with dichloroethane. Bulletin of Experimental Biology and Medicine 77:391-393.	190
5441619	Sergeev, S. N., Berezhnoi, R. V. (1977). Changes in distribution of carbonic-anhydrase activity in rat myocardium and liver during acute dichloroethane poisoning (histophotometric investigation). Bulletin of Experimental Biology and Medicine 83:108-110.	196
1776866	Zabrodskii, P.F., Germanchuk, V.G., Kirichuk, V.F., Nodel', M.L., Aredakov, A.N. (2003). Anticholinesterase mechanism as a factor of immunotoxicity of various chemical compounds. Bulletin of Experimental Biology and Medicine 136(2):176-178.	198
1048005	Zabrodskii, P.F., Troshkin, N.M., Mandych, V.G. (2004). Stimulation of immunotoxicity of chemicals metabolizing in vivo into highly toxic compounds by the monooxygenase system inductors. Bulletin of Experimental Biology and Medicine 138(4):369-371.	201
Short-term (>1-30 days)		
11728	Ghanayem, B. I., Maronpot, R. R., Matthews, H. B. (1986). Association of chemically induced forestomach cell proliferation and carcinogenesis. Cancer Letters 32(3):271-278.	203
Reproductive/Developmental		
62623	Vozovaia, M.A. (1977). [The effect of dichloroethane on the sexual cycle and embryogenesis of experimental animals]. Akusherstvo i Ginekologiya 2(2):57-59.	205

# **Isomer: dichloroethane**

Chronic (>91 days)

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18135 Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.

# **Isomer: 1,2-Dichloroethane**

#### Acute (less than or equal to 24 hr)

200247	Brondeau, M.T., Bonnet, P., Guenier, J.P., De, C.J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.	213
200279	Cottalasso, D., Domenicotti, C., Traverso, N., Pronzato, M., Nanni, G. (2002). Influence of chronic ethanol consumption on toxic effects of 1,2-dichloroethane: glycolipoprotein retention and impairment of dolichol concentration in rat liver microsomes and Golgi apparatus. Toxicology 178(3):229-240.	215
200280	Cottalasso, D., Fontana, L., Gazzo, P., Dapino, D., Domenicotti, C., Pronzato, M.A., Nanni, G. (1995). Effects of 1,2-dichloroethane intoxication on dolichol levels and glycosyltransferase activities in rat liver microsomes and Golgi apparatus. Toxicology 104(1-3):63-71.	217
194679	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J.A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. Mutagenesis 14(2):207-215.	219
10699112	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.	225
10699356	Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats.	233
2799602	Dow Chemical, (1989). Comparison of the acute lethality of selected hydrocarbons via intratracheal and oral routes (final report) with attachments, cover sheets and letter dated 061989.	238
5447286	Dow Chemical, (1962). Topical application of various solvents and solutions to evaluate dermal irritation.	242
625286	Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.	245
6570013	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).	249
725343	Dow Chemical, (1956). Results of skin absorption studies on carbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, trichloroethylene, and chlorothene.	267
60771	Francovitch, R.J., Schor, N.A., George, W.J. (1986). Effects of SKF 525A, phenobarbital, and 3-methylcholanthrene on ethylene dichloride toxicity following inhalation exposure. International Journal of Toxicology 5(2):117-126.	271
200352	Guo, X.L., Niu, Q. (2003). [The relationship between excitatory amino acids and acute intoxicated encephalopathy induced by 1,2-dichloroethane]. Zhonghua Laodong Weisheng Zhiyebing Zazhi / Chinese Journal of Industrial Hygiene and Occupational Diseases 21(2):83-85.	277
4528351	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.	279
6118	Kitchin, K.T., Brown, J.L., Kulkarni, A.P. (1993). Predicting rodent carcinogenicity of halogenated hydrocarbons by in vivo biochemical parameters. Birth Defects Research, Part B: Developmental and Reproductive Toxicology 13(4):167-184.	296

58151	Kronevi, T., Wahlberg, J.E., Holmberg, B. (1981). Skin pathology following epicutaneous exposure to seven organic solvents. International Journal of Tissue Reactions 3(1):21-30.	298
5540663	Livesey, J. C. (1982). Studies on the metabolism and toxicity of 1,2-dihaloethanes.	300
5447301	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.	302
200479	Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.	312
18954	Moody, D. E., James, J. L., Clawson, G. A., Smuckler, E. A. (1981). Correlations among the changes in hepatic microsomal components after intoxication with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693.	318
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62637	Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.	326
64411	Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.	328
200568	Salovsky, P., Shopova, V., Dancheva, V., Yordanov, Y., Marinov, E. (2002). Early pneumotoxic effects after oral administration of 1,2-dichloroethane. Journal of Occupational and Environmental Medicine 44(5):475-480.	332
200590	Sherwood, R.L., O'Shea, W., Thomas, P.T., Ratajczak, H.V., Aranyi, C., Graham, J.A. (1987). Effects of inhalation of ethylene dichloride on pulmonary defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.	334
62617	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.	338
6569955	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.	348
5549990	Storer, R. D., Conolly, R. B. (1983). Comparative in vivo genotoxicity and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-1494.	354
200613	Storer, R.D., Conolly, R.B. (1985). An investigation of the role of microsomal oxidative metabolism in the in vivo genotoxicity of 1,2-dichloroethane. Toxicology and Applied Pharmacology 77(1):36-46.	362
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4453007	Wang, G., Yuan, Y., Zhang, J., Gao, L., Tan, X., Yang, G., Lv, X., Jin, Y. (2014). Roles of aquaporins and matrix metalloproteinases in mouse brain edema formation induced by subacute exposure to 1,2-dichloroethane. Neurotoxicology and Teratology 44:105-112.	386
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Short-term (>1-30 days)		
200247	Brondeau, M.T., Bonnet, P., Guenier, J.P., De, C.J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.	400
5437237	Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology Journal 3:39-46.	403
62965	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477.	411
10609985	Dow Chemical, (2014). [Redacted] Investigation of the mode of action for 1,2-dichloroethane-induced mammary tumors in female F344/DuCrl rats.	425
625286	Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.	429
1772372	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.	433
200386	Igwe, O.J., Hee, S.S., Wagner, W.D. (1986). Interaction between 1,2-dichloroethane and disulfiram. I. Toxicologic effects. Fundamental and Applied Toxicology 6(4):733-746.	440
200387	Igwe, O.J., Hee, S.S., Wagner, W.D. (1986). Interaction between 1,2-dichloroethane and tetraethylthiuram disulfide (disulfiram). II. Hepatotoxic manifestations with possible mechanism of action. Toxicology and Applied Pharmacology 86(2):286-297.	444
5557200	Jin, X., Liao, Y., Tan, X., Guo, J., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of the p38 MAPK signaling pathway in overexpression of matrix metalloproteinase-9 during the course of brain edema in 1,2-dichloroethane-intoxicated mice. NeuroToxicology 69:296-306.	446
5431556	Jin, X., Liao, Y., Tan, X., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of CYP2E1 in the course of brain edema induced by subacute poisoning with 1,2-dichloroethane in mice. Frontiers in Pharmacology 9(1317):1317.	452
4492694	Li, W., Chen, L., Su, Y., Yin, H., Pang, Y., Zhuang, Z. (2015). 1,2-Dichloroethane induced nephrotoxicity through ROS mediated apoptosis in vitro and in vivo. Toxicology Research 4(5):1389-1399.	454
4309	Mccarty, L.P., Flannagan, D.C., Randall, S.A., Johnson, K.A. (1992). Acute toxicity in rats of chlorinated hydrocarbons given via the intratracheal route. Human & Experimental Toxicology 11(3):173-177.	456
62637	Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.	460
4697150	Pang, Y., Qi, G., Jiang, S., Zhou, Y., Li, W. (2018). 1,2-Dichloroethane induced hepatotoxicity and apoptosis by inhibition of ERK 1/2 pathways. Canadian Journal of Physiology and Pharmacology 96(11):1119-1126.	462

64411	Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.	464
200590	Sherwood, R.L., O'Shea, W., Thomas, P.T., Ratajczak, H.V., Aranyi, C., Graham, J.A. (1987). Effects of inhalation of ethylene dichloride on pulmonary defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.	466
62617	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.	470
4451633	Sun, Q., Wang, G., Gao, L., Shi, L., Qi, Y., Lv, X., Jin, Y. (2016). Roles of CYP2e1 in 1,2-dichloroethane-induced liver damage in mice. Environmental Toxicology 31(11):1430-1438.	478
1522109	Wang, G., Qi, Y., Gao, L., Li, G., Lv, X., Jin, Y.P. (2013). Effects of subacute exposure to 1,2-dichloroethane on mouse behavior and the related mechanisms. Human & Experimental Toxicology 32(9):983-991.	484
4453007	Wang, G., Yuan, Y., Zhang, J., Gao, L., Tan, X., Yang, G., Lv, X., Jin, Y. (2014). Roles of aquaporins and matrix metalloproteinases in mouse brain edema formation induced by subacute exposure to 1,2-dichloroethane. Neurotoxicology and Teratology 44:105-112.	486
5555689	Zeng, N., Jiang, H., Fan, Q., Wang, T., Rong, W., Li, G., Li, R., Xu, D., Guo, T., Wang, F., Zeng, L., Huang, M., Zheng, J., Lu, F., Chen, W., Hu, Q., Huang, Z., Wang, Q. (2018). Aberrant expression of miR-451a contributes to 1,2-dichloroethane-induced hepatic glycerol gluconeogenesis disorder by inhibiting glycerol kinase expression in NIH Swiss mice. Journal of Applied Toxicology 38(2):292-303.	492
5556105	Zhang, L., Jin, Y.P. (2019). Toxic effects of combined treatment of 1,2-dichloroethane and ethanol on mouse brain and the related mechanisms. Journal of Biochemical and Molecular Toxicology 33(5):1.	496
4453049	Zhang, Y., Li, G., Zhong, Y., Huang, M., Wu, J., Zheng, J., Rong, W., Zeng, L., Yin, X., Lu, F., Xie, Z., Xu, D., Fan, Q., Jia, X., Wang, T., Hu, Q., Chen, W., Wang, Q., Huang, Z. (2017). 1,2-dichloroethane induces reproductive toxicity mediated by the CREM/CREB signaling pathway in male NIH Swiss mice. Toxicological Sciences 160(2):299-314.	500
Subchronic (>30-91 days)		
194588	Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111.	506
62965	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477.	512
1772372	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.	525
1937626	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.	538
5447260	IRFMN, (1987). Report on the clinical chemistry results after 18 months inhalatory exposure - ethylene dichloride.	575
4528351	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.	579
200479	Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.	591

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62637	Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.	597
5441108	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.	601
1772371	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).	609
Chronic (>91 days)		
194588	Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111.	666
12097	Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.	675
94473	Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.	685
1937626	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.	691
5447359	IRFMN, (1976). Clinical chemistry results after 6 months inhalatory exposure to ethylene dichloride.	715
5447364	IRFMN, (1978). Clinical chemistry results in adult rats exposed to ethylene dichloride by inhalation for 12 months.	718
200427	Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice. Environmental Health Perspectives 69:89-95.	721
94773	Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice. Banbury Report 5:3-29.	736
1973131	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.	748
200497	Nagano, K., Umeda, Y., Senoh, H., Gotoh, K., Arito, H., Yamamoto, S., Matsushima, T. (2006). Carcinogenicity and chronic toxicity in rats and mice exposed by inhalation to 1,2-dichloroethane for two years. Journal of Occupational Health 48(6):424-436.	763
5441108	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.	769
62617	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.	797
200612	Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM transgenic mice. Carcinogenesis 16(2):285-293.	852
4451542	Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.	867

#### **Table of Contents** 1,1-Dichloroethane 194588 Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated furnigants in the rat diet. 885 Food and Cosmetics Toxicology 14(2):105-111. 62609 895 Lane, R.W., Riddle, B.L., Borzelleca, J.F. (1982). Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and development in mice. Toxicology and Applied Pharmacology 63(3):409-421. 12099 Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and 899 placental transfer of 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198. 5453539 911 Rao, K.S., Murray, J.S., Deacon, M.M., John, J.A., Calhoun, L.L., Young, J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylene dichloride. 5:P149-P166. 7310776 WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats. 919 200708 Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue 939 Zazhi 23(4):199-202. Other (specify) 94473 949 Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.

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Human Haalth Hagand A	nimal Toxicology Evaluation
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	8,

Study Citation: Health	Dow Chemic Mortality	cal, (1947). Results of range-finding toxicolo	ogical studi	es on Ethylidene Dichloride.
Outcome(s):	Wiortanty			
Reported Health	Mortality			
Effect(s):	Williamity			
Duration:	Acute (less t	han or equal to 24 hr) Acute-oral		
Chemical:		pethane- Parent compound		
HERO ID:	1973137	1		
Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The cover page of the submission specifies 1,1-dichloroethane was used. The study report names the test material as "ethylidine dichloride." A structural and empirical formula was provided.
	Metric 2:	Test Substance Source	Low	The test substance was from the Dow Chemical stockroom; it was not specified whether it was analytically verified.
	Metric 3:	Test Substance Purity	Low	The purity and/or grade were not reported.
D ' 0 T ' D '				
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	N/A	Not necessary for the study type
	Metric 5:	Positive Controls	N/A N/A	Not necessary for the study type  Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups
Domain 3: Exposure Cl	haracterization Metric 7:	Preparation and Storage of Test	Low	Information on preparation and storage was not reported. It is unclear whether a vehicle was used.
	Metric 8:	Substance Consistency of Exposure	Low	Details of exposure administration are insufficiently reported (e.g gavage volume)
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Results for two exposure doses were reported; it is unclear if other doses were tested.
	Metric 10:	Exposure Frequency and Duration	High	Single exposure (acute oral toxicity study)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The number of exposure groups is not explicitly stated. Based on the results, there were at least two dose groups.
	Metric 12:	Exposure Route and Method	Low	It is clear the exposure was oral, but it is not clear whether animals were dosed via gavage. Language in the text specifies "fed", but it is unlikely animals were dosed via their diet as this is not typical for an acute oral toxicity study.
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Low	The strain, sex, age, starting body weights, and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Low	The number of animals per group was not reported.
Di 5: 0 :				
Domain 5: Outcome As	Metric 16:	Outcome Assessment Methodology	Low	Animals were assessed for mortality, but it was not specified how long animals were observed post-exposure.

# Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

Study Citation: Health Dow Chemical, (1947). Results of range-finding toxicological studies on Ethylidene Dichloride.

lth Mortality

Outcome(s):

Reported Health

Mortality

Effect(s): Duration:

Acute (less than or equal to 24 hr) Acute-oral

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 1973137

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were not reported, but this is unlikely to have a substantial impact on study results
	Metric 18:	Sampling Adequacy	Low	Details of sampling were not reported.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the study type
	Metric 20:	Negative Control Response	N/A	Not applicable
Domain 6: Confoundi	ng / Variable Con Metric 21:	Confounding Variables in Test Design and Procedures	Low	No information to assess confounding was provided.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Not necessary for the study type
	Metric 24:	Reporting of Data	Low	Incidence data for each dose group were not provided. The cause or timing of death was not reported.

# **Overall Quality Determination**

## Low

Study Citation:	Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol)

Chemical: 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	Medium	Diethylnitrosamine was used as a positive control for the tumor initiation protocol.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure Ch	aracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	A single gavage dose appears sufficient for determination of tumor initiation potential (similar protocol used by Pereira et al., 1982).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only a single dose level was used, but it was justified as the MTD.
	Metric 12:	Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Damain 4. Tank Animala				
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment was appropriate and sensitive for tumor initiation potential.
	Metric 17:	Consistency of Outcome Assessment	High	Timing of necropsy was consistent across groups.
	Metric 18:	Sampling Adequacy	High	Sample size ( $n = 10$ ) was adequate for assessment of tumor initiation potential.
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Study Citation:		Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.						
Health	Cancer/Carcinogenesis							
<b>Outcome(s):</b>								
Reported Health	Increased inc	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)						
Effect(s):								
<b>Duration:</b>	Acute (less t	han or equal to 24 hr) Single dose (initiation	n protocol)					
Chemical:	1,1-Dichloro	ethane- Parent compound						
HERO ID:	200479							
Domain	Metric		Rating	Comments				
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology review.				
	Metric 20:	Negative Control Response	High	The biological response (incidence of GGT-positive foci) of the negative control group was adequate.				
Domain 6: Confoundi	ing / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	High	There is no evidence of confounding variables in test design and procedures that would affect tumor initiation.				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No animal attrition occurred in this experiment. There was no information either to sup- port or dismiss the suggestion that differences among groups in other health outcomes unrelated to exposure could influence the outcome assessment.				
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.				
	Metric 24:	Reporting of Data	High	Incidence data, with standard errors, are reported for each group in Table 3.				

1,1-Dichloroethane	Human Health Hazard Animal Toxicology Evaluation	HERO ID: 200479 Table: 2 of 3
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**Study Citation:** Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Nutritional/Metabolic Health

**Outcome(s):** 

Reported Health Decreased body weight gain (1,1,2-TCE only)

Effect(s):

Acute (less than or equal to 24 hr) Single dose (initiation protocol) **Duration:** 

**Chemical:** 1,1-Dichloroethane- Parent compound

HERO ID:	2004/9			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	N/A	A positive control is not required for the endpoint of body weight.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure Ch	naracterization			
r	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	A single gavage dose is appropriate for determination of acute effects.
	Metric 11:	Number of Exposure Groups and	Medium	Only a single dose level was used, but it was justified as the MTD.
		Dose/Concentration Spacing		
	Metric 12:	Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome As	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was appropriate. Body weight and body weight gain were measured.
	Metric 17:	Consistency of Outcome Assessment	Low	The timing of body weight measurements was not reported.
	Metric 18:	Sampling Adequacy	Low	Sample size for body weight and body weight gain was not reported.
	Metric 19:	Blinding of Assessors	N/A	The outcome (body weight) is not subjective.
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Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Decreased body weight gain (1,1,2-TCE only)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol)

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 200479

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	Low	The biological response (body weight) of the negative control group was not reported.
Domain 6: Confoundin	g / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Food and water were provided ad libitum. There is no evidence of confounding variables in test design and procedures that would affect the endpoint of body weight.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No animal attrition occurred in this experiment. There was no information either to sup- port or dismiss the suggestion that differences among groups in other health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described and the results were not shown.
	Metric 24:	Reporting of Data	Low	Results were described only in the text. Numerical values (i.e., body weight, body weight gain) were not provided.

# **Overall Quality Determination**

## Medium

HERO ID: 200479 Table: 3 of 3

**Study Citation:** Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health

Hepatic/Liver

**Outcome(s):** 

**Reported Health** 

Decreased absolute liver weight (1,1,2-TCE only)

Effect(s):

Acute (less than or equal to 24 hr) Single dose (initiation protocol) **Duration:** 

**Chemical:** 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substance	;			
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Design				
_	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	N/A	A positive control is not required for the endpoint of liver weight.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure Char	acterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	A single gavage dose is appropriate for determination of acute effects.
	Metric 11:	Number of Exposure Groups and	Medium	Only a single dose level was used, but it was justified as the MTD.
	wieure 11.	Dose/Concentration Spacing	Wicdiani	omy a single dose level was asea, but it was justified as the MTD.
	Metric 12:	Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome Asse	ccment			
	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment for liver was very limited (liver weight only).
	Metric 17:	Consistency of Outcome Assessment	High	Timing of necropsy was consistent across groups.
	Metric 18:	Sampling Adequacy	Low	Sample size for liver weight measurements was not reported.
	Metric 19:	Blinding of Assessors	N/A	The outcome (liver weight) is not subjective.
	Metric 20:	Negative Control Response	Low	The biological response (liver weight) of the negative control group was not reported.
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Human Health Hazard Animal Toxicology Evaluation HERO ID: 200479 Table: 3 of 3

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Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Hepatic/Liver

Outcome(s):

**Reported Health** Decreased absolute liver weight (1,1,2-TCE only)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol)

**Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 200479

Domain		Metric	Rating	Comments
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Food and water were provided ad libitum. There is no evidence of confounding variables in test design and procedures that would affect the endpoint of liver weight.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No animal attrition occurred in this experiment. There was no information either to support or dismiss the suggestion that differences among groups in other health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	Low	Results were described only in the text. Numerical values (i.e., absolute and relative liver weights) were not provided.

# **Overall Quality Determination**

# Medium

HERO ID: 644914 Table: 1 of 2

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Study Citation:	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.							
Health		l/Behavioral	Toxicological	Sciences 61(1).135 113.				
Outcome(s):								
Reported Health	CNS depression (excitation followed by progressive motor impairment and sedation) in acute study; No effects on CNS depression or brain weight in the							
Effect(s):	subacute study; Moderate CNS depression and no effects on brain weight or histopathology in the subchronic study.  Acute (less than or equal to 24 hr) Single dose							
Duration:								
Chemical:		pethane- Parent compound						
HERO ID:	644914	sediane Tarent compound						
Domain	0.1,71.	Metric	Rating	Comments				
Domain 1: Test Substance	re	Mone	rung	Commence				
Domain 1. Test buostant	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.				
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.				
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity.				
Domain 2: Test Design								
<u> </u>	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 5.1 mL.				
	Metric 5:	Positive Controls	N/A	Positive controls are not necessary in an acute toxicity study.				
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.				
Domain 3: Exposure Cha								
	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.				
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.				
	Metric 9:	Reporting of Doses/Concentrations	High	Nominal dosages were reported, but in a gavage study analytical concentrations are not necessary.				
	Metric 10:	Exposure Frequency and Duration	High	Animals were given a single dose via oral gavage, and monitored for 2 weeks following treatment.				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.				
	Matria 12	Evenous Pouts and Mathad	High	The test only the control of the con				

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High

High

The test substance was administered by gavage in corn oil.

Sex, strain, and species were reported. In the acute study, the rats were male and weighed 250-300 g. Rats were obtained from Harlan (Indianapolis, IN).

Exposure Route and Method

Test Animal Characteristics

Metric 12:

Metric 13:

Domain 4: Test Animals

		continu	ied from previ	ous page			
Study Citation:  Health Outcome(s):	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. Neurological/Behavioral						
Reported Health Effect(s): Duration: Chemical: HERO ID:	subacute stud Acute (less t	sion (excitation followed by progressive motody; Moderate CNS depression and no effects han or equal to 24 hr) Single dose bethane- Parent compound		nd sedation) in acute study; No effects on CNS depression or brain weight in the t or histopathology in the subchronic study.			
Domain		Metric	Rating	Comments			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.			
	Metric 15:	Number of Animals per Group	Medium	Groups of 8 rats were used in the acute study.			
Domain 5: Outcome As	seessment						
Domain 3. Outcome As	Metric 16:	Outcome Assessment Methodology	Low	The method for assessing CNS depression was not reported. Excitation, progressive motor impairment, and sedation were reported in the results.			
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding execution of the outcome assessment were not provided. The sedation was reported to be dose-dependent. It was not stated if the same protocol was used for all study groups.			
	Metric 18:	Sampling Adequacy	Low	The number of animals sampled per group was not reported (the outcome assessment methodology was not reported), but is not likely to affect the results.			
	Metric 19:	Blinding of Assessors	Medium	The study did not report whether the assessors were blinded, but lack of blinding is not expected to have a substantial impact on results.			
	Metric 20:	Negative Control Response	High	Rats receiving less than or equal to 2000 mg/kg bw were not reported to have CNS depression.			
Domain 6: Confounding	g / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure. Health outcomes could be attributed to exposure based on dose-dependency.			
	Metric 23:	Data Presentation and Analysis	Low	General approaches to statistical analysis were clearly described, but it is not clear whether these methods were applied for CNS depression.			
	Metric 24:	Reporting of Data	Low	Presence and severity of CNS depression were only summarized qualitatively in the text. The authors state that the "magnitude and duration of sedation were dose-dependent" and observed in doses of 2g/kg and above, but do not provide detailed information on incidence, duration and severity of CNS depression in each dose group.			

### **Overall Quality Determination**

## Medium

HERO ID: 644914 Table: 2 of 2

**Study Citation:** Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. Health Mortality **Outcome(s):** 

**Reported Health** 

The number of deaths per treatment group. **Effect(s):** 

**Duration:** Chemical: Acute (less than or equal to 24 hr) Single dose 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity
Domain 2: Test Design				
Bollium 2. Test Besign	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 5.1 mL.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Ch	aracterization			
Zoman or Ziposare cir	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Medium	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent across treatment groups and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	High	Nominal dosages were reported, but in a gavage study analytical concentrations are not necessary.
	Metric 10:	Exposure Frequency and Duration	High	A single dose was administered in the acute study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The exposure levels were not justified in the paper, but the selected range sufficiently covered the full range of responses.
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4: Test Animals				
Domain 4. Test Allilliais	Metric 13:	Test Animal Characteristics	Medium	Sex, strain, and species were reported. In the acute study, the rats were male and weighed 250-300 g. Rats were obtained from Harlan (Indianapolis, IN).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.
	Metric 15:	Number of Animals per Group	Medium	Groups of 8 rats were used in the acute study.

HERO ID: 644914 Table: 2 of 2

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**Study Citation:** Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

**Outcome(s):** 

**Reported Health** 

The number of deaths per treatment group.

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single dose

Chemical: 1,1-Dichloroethane- Parent compound

Mortality

**HERO ID:** 644914

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	The number of deaths that occurred within 2 weeks was recorded.
Metric 17:	Consistency of Outcome Assessment	High	Samples were collected at sacrifice.
Metric 18:	Sampling Adequacy	High	Survival/mortality was recorded for all individuals.
Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary.
Metric 20:	Negative Control Response	High	There were 0 deaths in the control group.
Domain 6: Confounding / Variable Co Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables were recorded. Body weight was reported, but food and drinking water consumption were not reported.
Metric 21:	2	High High	
	Exposure	111811	mg/kg bw, and 4000 mg/kg bw; 4/8 at 8000 mg/kg bw, 5/8 at 12000 mg/kg bw, and 8/8 at 16000 mg/kg bw.
Metric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.
Metric 24:	Reporting of Data	High	Negative findings were reported qualitatively. Positive findings were reported in tables or graphs.

# **Overall Quality Determination**

# High

Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44.

Health Renal/Kidney

**Outcome(s):** 

**Study Citation:** 

Reported Health

Urinary glucose and protein; renal histopathology

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- single dose

Chemical: 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure Cha	aracterization			
Zomani di Ziipodai e dii	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration are incomplete.
	Metric 9:	Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and	Medium	There were minor limitation in dose spacing.
		Dose/Concentration Spacing		
	Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The source and age of the mice was not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed/group was not reported as 10 in each group (Table 4 legend).
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Some details regarding the outcome assessment methodology were lacking (e.g how long urine was collected for).
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
		Coi	ntinued on next page .	

continue	ed from previous page

Study Citation: Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health

Urinary glucose and protein; renal histopathology

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute- single dose

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 64411

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	Medium	The sampling was adequate (all surviving mice)
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.
	Metric 20:	Negative Control Response	High	Negative control responses for urinary parameters were reported in text and were appropriate for some outcomes.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Low	Statistics analysis were not performed. Significance of increased urinary glucose or protein was determined by a cutoff number set by the authors.
	Metric 24:	Reporting of Data	Medium	Incidence data is provided for presence of urinary glucose or protein above cutoff level.  The measured level of glucose and protein would be more useful.

# **Overall Quality Determination**

# Uninformative

HERO ID: 64411 Table: 2 of 2

Study Citation: Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44.

Health

Mortality

**Outcome(s):** 

Reported Health

Mortality

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- single dose

Chemical: 1,1-Dichloroethane- Parent compound

HERO ID.	01111			
Domain		Metric	Rating	Comments
Domain 1: Test Substa	ance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Desig	n			
	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is info mation on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure (	Tharacterization			
Bomain 3. Exposure v	Metric 7:	Preparation and Storage of Test	Low	Preparation and storage conditions were not properly reported given the volatility of the
		Substance		test substance.
	Metric 8:	Consistency of Exposure	Medium	Details of exposure administration are incomplete.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and	Medium	There were minor limitation in dose spacing.
		Dose/Concentration Spacing		
	Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Low	The source and age of the mice was not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed/group was not reported as 10 in each group (Table 4 legend).
Domain 5: Outcome A	seecement			
Domain J. Outcome F	Metric 16:	Outcome Assessment Methodology	Medium	Details regarding the outcome assessment methodology were lacking.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Medium	The sampling was adequate.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.
	Wichie 19.	Diffiding of Assessors	IVA	Dimaing was not necessary for outcomes studied.

HERO ID: 64411 Table: 2 of 2

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Study Citation: Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44.

Health

Mortality

**Outcome(s):** 

Reported Health

Mortality

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute- single dose

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 64411

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	Low	Negative control responses was not reported.
Domain 6: Confounding	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistics analysis were not performed but data is presented so that independent analysis can be done.
	Metric 24:	Reporting of Data	High	Mortality data is adequately presented.

# **Overall Quality Determination**

# Uninformative

HERO ID: 644914 Table: 1 of 8

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Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

**Health** Mortality

**Outcome(s):** 

**Reported Health** The number of deaths per treatment group.

Effect(s):

**Duration:** Short-term (>1-30 days) 10 days **Chemical:** 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
Me	etric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
Me	etric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
Me	etric 3:	Test Substance Purity	High	Reported as 99.99% purity.
Domain 2: Test Design				
	etric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 5.1 mL.
Me	etric 5:	Positive Controls	N/A	Positive controls are not necessary in the subacute study.
Me	etric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characte	terization			
-	etric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
Ме	etric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
Me	etric 9:	Reporting of Doses/Concentrations	High	Nominal dosages were reported, but analytical concentrations are not necessary since this was an oral gavage study.
Me	etric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for 1, 5 or 10 days.
Me	etric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The exposure levels were not justified in the paper, but the selected range sufficiently covered the full range of responses.
Me	etric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4: Test Animals				
	etric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subacute, the rats were male and weighed 250-300 g. The animals were obtained from Harlan (Indianapolis, IN).
Me	etric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.

HERO ID: 644914 Table: 1 of 8

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Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

The number of deaths per treatment group.

**Effect(s):** 

**Duration:**Short-term (>1-30 days) 10 days**Chemical:**1,1-Dichloroethane- Parent compound

**HERO ID:** 644914

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	Groups of 8 rats were used in the subacute study.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Mortality was measured as # of deaths.
	Metric 17:	Consistency of Outcome Assessment	High	Samples were collected at sacrifice.
	Metric 18:	Sampling Adequacy	High	All animals were observed for mortality.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary.
	Metric 20:	Negative Control Response	High	The control group did not exhibit any mortality.
Domain 6: Confound	ing / Variable Cor Metric 21:	Confounding Variables in Test Design	Medium	The study did not provide sufficient information to determine potential for confounding,
		and Procedures		but no differences among groups were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Low	LD50 was estimated using Litchfield and Wilcoxon method but it is not clear whether statistical analysis was performed for deaths in the subacute study.
	Metric 24:	Reporting of Data	Low	The number of deaths within 24 hours was described in the text for the high dose group. The lack of mortality in lower dose groups or later timepoints is implied but not clearly stated.

# **Overall Quality Determination**

High

<b>Study Citation:</b>	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of
	1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.
Haalth	Immuna // Immatala giaali Dama duativa /Davalammantali

Health

**Effect(s):** 

Immune/Hematological; Reproductive/Developmental;

Outcome(s): Reported Health

Immune/Hematological: No effects on histopathology or organ weight of the spleen; Reproductive/Developmental: No histopathological effects on testis

or epididymis;

**Duration:** Short-term (>1-30 days) 10 days **Chemical:** 1,1-Dichloroethane- Parent compound **HERO ID:** 644914

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metri	c 1: Test Substance Identity	High	All Outcomes: The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
Metri	c 2: Test Substance Source	High	All Outcomes: Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
Metri	c 3: Test Substance Purity	High	All Outcomes: Reported as 99.99% purity.
Domain 2: Test Design			
Metri	c 4: Negative and Vehicle Controls	High	All Outcomes: Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 5.1 mL.
Metri	c 5: Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.
Metri	c 6: Randomized Allocation of Anima	ls Medium	All Outcomes: The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characteri	zation		
Metri		Medium	All Outcomes: Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
Metri	c 8: Consistency of Exposure Administration	Low	All Outcomes: The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
Metri	c 9: Reporting of Doses/Concentration	s High	All Outcomes: Nominal doses were reported, but analytical concentrations were not necessary based on oral gavage.
Metri	c 10: Exposure Frequency and Duration	High	All Outcomes: Doses were administered the test substance once daily for up to 10 days.
Metri	c 11: Number of Exposure Groups Dose/Concentration Spacing	_	All Outcomes: The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
Metri		High	All Outcomes: The test substance was administered by gavage in corn oil.
Domain 4: Test Animals			
Metri	c 13: Test Animal Characteristics	High	All Outcomes: Sex, strain, and species were reported. In the subacute study, the rats

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Study Citation:	1,1-dichloro	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. Immune/Hematological; Reproductive/Developmental;							
Outcome(s):									
Reported Health	Immune/Her	natological: No effects on histopathology of	or organ wei	ght of the spleen; Reproductive/Developmental: No histopathological effects on testi					
Effect(s):		or epididymis;							
Duration:		Short-term (>1-30 days) 10 days							
Chemical:		bethane- Parent compound							
HERO ID:	644914	•							
Domain		Metric	Rating	Comments					
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.					
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: Groups of 8 rats were used in the subacute study.					
Domain 5: Outcome A	Assessment								
Domain 3. Gateome 1	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Clinical chemistry, organ weight, and histopathology was performed for all treatment groups.					
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome assessment was consistent for all treatment groups					
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Samples were collected from all animals, but it was not reported how many were evaluated per group.					
	Metric 19:	Blinding of Assessors	High	All Outcomes: For histopathology, the study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.					
	Metric 20:	Negative Control Response	High	Immune/Hematological: The control group did not exhibit any abnormal spleen effects.; Reproductive/Developmental: The control group did not exhibit any abnormal testis or epididymis effects.					
Domain 6: Confoundi	ng / Variable Co	ntrol							
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.					
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.					
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.					
	Metric 24:	Reporting of Data	High	All Outcomes: Negative findings were reported qualitatively.					
Overall Qual	ity Detern	nination	High						

Study Citation:		a, S., Ramanathan, R., Mehta, S.M., pethane in rats: Application to risk ev		a, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of gical Sciences 64(1):135-145.			
Health	Renal/Kidn	Renal/Kidney					
Outcome(s):							
Reported Health	No effect or	n relative kidney weight or clinical cl	hemistry in acute st	tudy; In the subacute study, elevated kidney NSPH was reported after 5 and 10 days in			
Effect(s):	the 2 and 4 g/kg dose groups. In the subchronic study, urinary elimination of ACP and NAG significantly increased at 8 weeks of exposure in the 1, 2 and 4 g/kg exposure groups, and ACP significantly decreased relative to control at 12 weeks, but there was no effect on kidney weight, clinical chemistry, or histopathology.						
Duration:	Short-term	(>1-30 days) 10 days					
Chemical:	1,1-Dichlor	oethane- Parent compound					
HERO ID:	644914						
Domain		Metric	Rating	Comments			
Domain 1: Test Subst	ance						
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.			
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verifica- tion was not mentioned, and a batch or lot number were not provided.			
				tion was not includicu, and a batch of lot number were not provided.			

Domain 1. Test Substant				
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 5.1 mL.
	Metric 5:	Positive Controls	N/A	Positive controls are not needed based on the study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
D : 3 E G	, . ,.			
Domain 3: Exposure Cha		D (1.0) CT (	3.6.11	
	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	High	Nominal doses were reported, but analytical concentrations were not needed based on it being an oral gavage study.
	Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for 1, 5, or 10 days.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4. Test Asimala				
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subacute study, the rats were male and weighed 250-300 g. The animals were obtained from Harlan (Indianapolis, IN).

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Study Citation: Health	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity stu 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. Renal/Kidney				
Outcome(s):					
Reported Health				udy; In the subacute study, elevated kidney NSPH was reported after 5 and 10 days in	
Effect(s):	the 2 and 4 g/kg dose groups. In the subchronic study, urinary elimination of ACP and NAG significantly increased at 8 weeks of expc 4 g/kg exposure groups, and ACP significantly decreased relative to control at 12 weeks, but there was no effect on kidney weight, cl				
	4 g/kg expos		ea relative to	o control at 12 weeks, but there was no effect on kidney weight, clinical chemistry, or	
Duration:		gy. >1-30 days) 10 days			
Chemical:		pethane- Parent compound			
HERO ID:	644914	ration compound			
Domain		Metric	Rating	Comments	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.	
	Metric 15:	Number of Animals per Group	Medium	Groups of 8 rats were used in the subacute study.	
Domain 5: Outcome A	Assessment Metric 16:	Outcome Assessment Methodology	High	Clinical chemistry, organ weight, and histopathology was performed for all treatment groups.	
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent for all treatment groups	
	Metric 18:	Sampling Adequacy	Medium	Kidney weights and urinalysis endpoints were evaluated for 8 rats/group at each time- point. For histopathology, samples were collected from all animals, but it was not re- ported how many were evaluated per group.	
	Metric 19:	Blinding of Assessors	High	For kidney histopathology, the study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.	
	Metric 20:	Negative Control Response	High	The control group did not exhibit any adverse kidney effects.	
Di- (. Cf1:	/ W: -b-1- C	1			
Domain 6: Confounding	Metric 21:	Confounding Variables in Test Design	Medium	The study did not mayide sufficient information to determine notantial for confounding	
	Metric 21.	and Procedures	Mediuiii	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.	
	Metric 22:	Health Outcomes Unrelated to	High	There was no information either to support or dismiss the suggestion that there were	
		Exposure	C	differences among groups in animal attrition or health outcomes unrelated to exposure.	
	Metric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.	
	Metric 24:	Reporting of Data	High	Findings were reported qualitatively and quantitatively in Table 1 and Table 2.	
Overall Qual	ity Detern	nination	High		

HERO ID: 644014 Table	. 1 of 0

Study Citation:	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of
	1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Hepatic/Liver

**Outcome(s): Reported Health** 

Decreased absolute and relative liver weight in subacute study; no effects on clinical chemistry in acute or subchronic studies; no effects on liver weight in subchronic study, but authors report a slight difference in hepatocyte histology (mild condensation and a change in cytoplasmic staining consistent with glycogen mobilization) in survivors sacrificed at 11 weeks.

**Duration:** Chemical:

**Effect(s):** 

Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Parent compound

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
Metric 3:	Test Substance Purity	High	Reported as 99.99% purity
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from $0.15$ to $5.1$ mL.
Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characterizatio	n		
Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
Metric 9:	Reporting of Doses/Concentrations	High	Nominal doses were reported, but analytical concentrations were not necessary based on oral gavage.
Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for up to 10 days.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
Metric 12:		High	The test substance was administered by gavage in corn oil.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subacute study, the rats were male and weighed 250-300 g. The animals were obtained from Harlan (Indianapolis, IN).
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.

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Study Citation:	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.					
Health	Hepatic/Liver					
Outcome(s):						
Reported Health	Decreased a	Decreased absolute and relative liver weight in subacute study; no effects on clinical chemistry in acute or subchronic studies; no effects on liver weight				
Effect(s):	in subchronic study, but authors report a slight difference in hepatocyte histology (mild condensation and a change in cytoplasmic staining consistent wi					
	glycogen mobilization) in survivors sacrificed at 11 weeks.					
Duration:	Short-term (>1-30 days) 10 days					
Chemical:	1,1-Dichloro	pethane- Parent compound				
HERO ID:	644914					
Domain		Metric	Rating	Comments		
	Metric 15:	Number of Animals per Group	Medium	Groups of 8 rats were used in the subacute study.		
Domain 5: Outcome	Metric 16:  Metric 17: Metric 18:  Metric 19:  Metric 20:	Outcome Assessment Methodology  Consistency of Outcome Assessment Sampling Adequacy  Blinding of Assessors  Negative Control Response	High High Medium High High	Clinical chemistry, liver weight, and histopathology was performed for all treatment groups.  Outcome assessment was consistent for all treatment groups  Liver weights and clinical chemistry were evaluated for 8 rats/group at each timepoint.  For liver histopathology, samples were collected from all animals, but it was not reported how many were evaluated per group.  For histopathology, the study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.  The control group did not exhibit any abnormal liver effects.		
Domain 6: Confound	ing / Variable Con	ntrol				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although body weight was significantly reduced, the effects on liver weight were still significant (relative and absolute). No confounding variables were reported.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.		
	Metric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.		
	Metric 24:	Reporting of Data	High	Findings were reported qualitatively and quantitatively in Table 1 and Table 2.		
Overall Quality Determination			High			

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. Nutritional/Metabolic

Health

**Outcome(s): Reported Health** 

Reduced body weight gain in subacute and subchronic studies

**Effect(s):** 

Short-term (>1-30 days) 10 days **Duration:** Chemical: 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substanc	e			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 5.1 mL.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Cha	racterization			
Bonium 3. Exposure ene	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	High	Nominal dosages were reported, but analytical concentrations were not required for a gavage study.
	Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily 1, 5, and 10 days.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4: Test Animals				
Domain 4: Test Ammais	Metric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subacute study, the rats were male and weighed 250-300 g. The animals were obtained from Harlan (Indianapolis, IN).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.
	Metric 15:	Number of Animals per Group	Medium	Groups of 8 rats were used in the subacute study.

HERO ID: 644914 Table: 5 of 8

#### ... continued from previous page

**Study Citation:** Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Reduced body weight gain in subacute and subchronic studies

Effect(s): **Duration:** Chemical:

Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 5: Outcome Assessm	ent			
	tric 16:	Outcome Assessment Methodology	High	Body weight measurements were taken.
	tric 17:	Consistency of Outcome Assessment	High	Body weights were measured for all treatment groups
	tric 18:	Sampling Adequacy	Medium	Although not specifically stated, it is assumed that examination of body weight was performed for all animals. Authors report that each data point represents body weight measurements for groups of 8-16 rats.
Me	tric 19:	Blinding of Assessors	N/A	Blinding was not necessary.
Met	tric 20:	Negative Control Response	High	The control group did not exhibit any abnormal body weight effects.
Domain 6: Confounding / Var Met	riable Cor tric 21:	ntrol Confounding Variables in Test Design and Procedures	Medium	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
Met	tric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Met	tric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA to evaluate the statistical significance of DCE-induced changes.
Met	tric 24:	Reporting of Data	Medium	Body weight data and statistical significant for the subacute study were reported graphically and described in the text.
Overall Quality Determination		High		

HERO ID: 644914 Table: 6 of 8

Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Adrenal (Adrenal)

**Outcome(s):** 

Reported Health

Adrenals histopathology were evaluated and no effects were found.

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 10 days **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 644914

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity.
Domain 2: Test Design				
2 0 21 1000 2 001g.	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from $0.15$ to $5.1$ mL.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Ch	aracterization			
Zomani J. Exposure Ci	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only nominal dosages were reported.
	Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for up to 10 days.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4: Test Animals				
2 chair ii root i iiiiiidi	Metric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subacute study, the rats were 250-300 g. The animals were obtained from Harlan (Indianapolis, IN).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.
	Metric 15:	Number of Animals per Group	Medium	Groups of 8 rats were used in the subacute study.

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Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Outcome(s):

**Reported Health** 

Adrenals histopathology were evaluated and no effects were found.

**Effect(s):** 

**Duration:**Short-term (>1-30 days) 10 days**Chemical:**1,1-Dichloroethane- Parent compound

Adrenal (Adrenal)

	Metric	Rating	Comments
sessment			
Metric 16:	Outcome Assessment Methodology	High	Clinical chemistry, organ weight, and histopathology was performed for all treatment groups.
Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent for all treatment groups
Metric 18:	Sampling Adequacy	Low	Samples were collected from all animals, but it was not reported how many were evaluated per group.
Metric 19:	Blinding of Assessors	High	The study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.
Metric 20:	Negative Control Response	High	The control group did not exhibit any abnormal adrenal effects.
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although body weight was significantly reduced, this is not expected to affect the interpretation of the results. The study did not provide sufficient information to determine other potential sources of confounding, but no differences among groups were reported.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Metric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.
Metric 24:	Reporting of Data	High	Negative findings were reported qualitatively.
	Metric 17: Metric 18: Metric 19: Metric 20: g / Variable Con Metric 21: Metric 22:	Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  7 / Variable Control Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure	Metric 16: Outcome Assessment Methodology High  Metric 17: Consistency of Outcome Assessment High Metric 18: Sampling Adequacy Low  Metric 19: Blinding of Assessors High  Metric 20: Negative Control Response High  g / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure

HERO ID: 644914 Table: 7 of 8

Study Citation:

Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health
Outcome(s):

Reported Health
Effect(s):

CNS depression (excitation followed by progressive motor impairment and sedation) in acute study; No effects on CNS depression or brain weight in the subchronic study.

**Duration:** Short-term (>1-30 days) 10 days **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 644914

Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			20
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity.
Domain 2: Test Desi	ion			
Domain 2. Test Besi	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from $0.15$ to $5.1$ mL.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure	Characterization			
Domain 3. Exposure	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The dose were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only nominal dosages were reported.
	Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for up to 10 days.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4: Test Anii	mals			
	Metric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subacute, the rats were 250-300 g. The animals were obtained from Harlan (Indianapolis, IN).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.
	Metric 15:	Number of Animals per Group	Medium	Groups of 8 rats were used in the subacute study.

#### Continued on next page ...

HERO ID: 644914 Table: 7 of 8

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Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health Neurological/Behavioral

**Outcome(s):** 

Reported Health Effect(s):

CNS depression (excitation followed by progressive motor impairment and sedation) in acute study; No effects on CNS depression or brain weight in the

subacute study; Moderate CNS depression and no effects on brain weight or histopathology in the subchronic study.

**Duration:** Short-term (>1-30 days) 10 days **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 644914

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric	16: Outcome Assessment Methodology	Low	Methodology was not reported for CNS depression.
Metric	17: Consistency of Outcome Assessment	Low	Methodology was not reported for CNS depression, making it difficult to determine whether assessment was consistent across groups.
Metric	18: Sampling Adequacy	Low	Details of sampling for this endpoint are not reported.
Metric	19: Blinding of Assessors	Medium	The study did not report whether the assessors were blinded, but lack of blinding is not expected to have a substantial impact on results.
Metric	20: Negative Control Response	High	The control group did not exhibit any CNS effects.
Domain 6: Confounding / Variab	le Control		
Metric	21: Confounding Variables in Test Design and Procedures	Medium	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
Metric	22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Metric	*	Low	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test, but it is not clear whether any statistical analysis if any was performed on CNS depression.
Metric	24: Reporting of Data	Low	Findings were reported qualitatively.

# **Overall Quality Determination**

# Medium

Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Lung/Respiratory

**Outcome(s):** 

Reported Health Effect(s):

In the acute study, mild focal pneumonitis was "occasionally seen in the lungs of animals, particularly in controls"; pulmonary inflammation was evaluated in the subchronic study and was observed in both control and treated animals.

Duration: Chemical: HERO ID: Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Parent compound

644914

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 5.1 mL.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Ch	naracterization			
Domain 3. Exposure Cr	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only nominal dosages were reported.
	Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for up to 10 days.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4: Test Animals	s.			
Domain 7. Test / Millian	Metric 13:	Test Animal Characteristics	Medium	Sex, strain, and species were reported. In the subacute study, the rats were 250-300 g. The animals were obtained from Harlan (Indianapolis, IN).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in
		,		negative flow care racks in a temperature- and humidity-controlled biohazard suite.

**Study Citation:** Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. Lung/Respiratory

Health

**Outcome(s):** 

**Reported Health** Effect(s):

In the acute study, mild focal pneumonitis was "occasionally seen in the lungs of animals, particularly in controls"; pulmonary inflammation was evaluated in the subchronic study and was observed in both control and treated animals.

Negative findings were reported qualitatively.

**Duration:** Short-term (>1-30 days) 10 days Chemical: 1,1-Dichloroethane- Parent compound **HERO ID:** 644914

Metric 24:

Domain		Metric	Rating	Comments
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Clinical chemistry, organ weight, and histopathology was performed for all treatment groups.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent for all treatment groups
	Metric 18:	Sampling Adequacy	Low	Samples were collected from all animals, but it was not reported how many were evaluated per group.
	Metric 19:	Blinding of Assessors	High	The study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.
	Metric 20:	Negative Control Response	High	The control group did not exhibit any abnormal pulmonary effects.
Domain 6: Confound	ding / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Although body weight was significantly reduced, this is not expected to affect the interpretation of the results
	Metric 22:	Health Outcomes Unrelated to Exposure	High	There were no effects reported that could not be attributed to treatment.
	Metric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.

High

#### **Overall Quality Determination** High

Reporting of Data

Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44. Renal/Kidney

Health Renal/Kidney

**Outcome(s):** 

**Study Citation:** 

Reported Health

Urinary glucose and protein; renal histopathology

Effect(s):

**Duration:** Short-term (>1-30 days) Short-term- 3 days **Chemical:** 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	Medium	Details of exposure administration are incomplete.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and	Medium	The one dose studied was the highest one that did not cause lethality.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	Route of exposure was i.p. injection.
Domain 4: Test Animals	1			
	Metric 13:	Test Animal Characteristics	Low	The source and age of mice were not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Low	The number of animals/group were not reported.
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	Low	Some details regarding the outcome assessment methodology were lacking (e.g how long urine was collected for, histological evaluations)
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Uninformative	Histology was not performed on controls.
		Con	ntinued on next page .	

Study Citation: Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44.

Health

Renal/Kidney

**Outcome(s):** 

**Reported Health** 

Urinary glucose and protein; renal histopathology

**Effect(s):** 

**Duration:** Short-term (>1-30 days) Short-term- 3 days **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 64411

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.
	Metric 20:	Negative Control Response	Low	Negative control histology was not reported.
Domain 6: Confounding	ng / Variable Co	ntrol Confounding Variables in Test Design	Low	Potential confounding variables were not reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to	Medium	There was no information either to support or dismiss the suggestion that there were
		Exposure		differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed; independent statistics could be done.
	Metric 24:	Reporting of Data	Low	Combistix analysis data were not presented.

# **Overall Quality Determination**

### Uninformative

Study Citation:	Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in
Study Citation.	believel, B.R., Beong, B.R., Centing, 1.3. (1771). Emoly and recording of inhaled carbon terraemorate, 1,1 demoloculare and methyl entry records in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health Hepatic/Liver

Outcome(s): Reported Health

Liver weights, gross appearance/pathology and SGPT/ALT activity

Effect(s):

**Duration:**Short-term (>1-30 days) 10 days**Chemical:**1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1: Metric 2:	Test Substance Identity Test Substance Source	High High	The test substance was specified clearly by chemical name (1,1-dichloroethane).  The source of the test substance was reported and included a lot number.
	Metric 3:	Test Substance Purity	High	Reagent-grade 1,1-dichloroethane was used. However, an analysis of the test material was performed, indicating that the volume of 1,1-dichloroethane by weight in the sample was 99.7% (other minor sample components were shown in Table 2).
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	The study reports that animals were exposed to 1,1-dichloroethane at two different concentrations, one in an initial experiment and another in a subsequent experiment. For each experiment, control animals were exposed concurrently to filtered air.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The manner by which animals were allocated to study groups was not reported.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	The vapor generation process was briefly outlined ("generated by metering liquid at known rates into a temperature-controlled evaporating flask"). Storage conditions of the (volatile) test substance were not reported. Owing to methods used to ensure that proper exposure concentrations were maintained throughout the study, missing details are unlikely to have a substantial impact on the study results.
	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration suggest that animals were exposed consistently across study groups (7 hours/day for 10 days in dynamic chambers). The time of day exposures were administered was not reported; language in the report suggests exposures were simultaneous.
	Metric 9:	Reporting of Doses/Concentrations	High	Analytical, nominal, and target concentrations were reported. Analytical concentrations were measured 3 times during each daily exposure (for 10 days) by spectrophotometry; the mean of these measurements resulted in analytical concentrations within 10% of the nominal concentrations. Combustion conductivity analyses was also used to continuously monitor concentrations.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration (the same for each experiment) were reported (i.e., 7 hours/day for 10 days) and appropriate for evaluating the outcome of interest. Daily exposures slightly longer than the standard from applicable guidelines (6 hours/day) was not considered a study limitation.
		Cont	inued on next pa	nge

Study Citation: Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

Hepatic/Liver

**Outcome(s):** 

Reported Health

Liver weights, gross appearance/pathology and SGPT/ALT activity

Effect(s):

**Duration:** Short-term (>1-30 days) 10 days **Chemical:** 1,1-Dichloroethane- Parent compound

HERO ID:	62395			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	There were deficiencies in the number of dose groups utilized; two experiments were conducted, each using one 1,1-dichloroethane exposure group. No rationale for the exposure concentrations were provided other than "subanesthetic concentrations" were used.
	Metric 12:	Exposure Route and Method	Medium	A dynamic whole-body chamber was used for vapors; the number of changes per hour was not reported.
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Low	The source of the test animals was not reported. The species and strain, life-stage, and approximate starting body weights of the test animals was indicated.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not explicitly specified; the study report indicates that between exposures, animals were housed in cages, provided food and water ad libitum, and that the room was controlled for other factors (temperature, humidity, and light/dark cycle, not further specified).
	Metric 15:	Number of Animals per Group	Medium	It appears that 10 animals/group were used (i.e., exposed to 1,1-dichloroethane); this number is appropriate for studies of this type.
Domain 5: Outcome A	Scacemant			
Boniani 3. Outcome A	Metric 16:	Outcome Assessment Methodology	Medium	The methods used evaluated liver toxicity by measuring SGPT/ALT activity, liver weights, and gross pathology. Liver histology was not performed. Some liver measurements were recorded 6 days after cessation of treatment.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups (i.e., liver effects were assessed at the same time points).
	Metric 18:	Sampling Adequacy	Medium	Based on a study referenced in this report (HEROID 65020) and data provided in tables, liver endpoints were evaluated in all animals (e.g., SGPT/ALT activity was measured in all 10 animals/group during the study). However, relative liver weights immediately after exposure were based on 4 animals/group only; SGPT/ALT activity and relative liver weights were measured for the remaining 6 animals/group 6 days after the last exposure.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not required by study type; outcomes were not subjective.
	Metric 20:	Negative Control Response	Medium	The biological responses of the negative control shown were adequate. There were presumably no effects on gross pathology in controls.
Domain 6: Confoundi	ng / Variable Co	ntrol		
Domain o. Comound	Metric 21:	Confounding Variables in Test Design	Medium	Although not all data were reported on confounding, the available data did not identify
		and Procedures	1.10010111	differences among groups.
		Contin	ued on next pa	nge

HERO ID: 62395 Table: 1 of 1

#### ... continued from previous page

Study Citation: Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464. Hepatic/Liver

Health

Outcome(s): Reported Health

Liver weights, gross appearance/pathology and SGPT/ALT activity

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 10 days **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 62395

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Reported data do not indicate that health outcomes unrelated to exposure influenced the study results.
	Metric 23:	Data Presentation and Analysis	High	Statistical analyses were briefly described in the cited reference (HEROID 65020). Liver endpoints were analyzed by an analysis of variance and Dunnett's test or Tukey's test.
	Metric 24:	Reporting of Data	Low	It is not clear if two separate control groups were used, and the amount of time between experiments was not specified. Data for SGPT/ALT activity and liver weights were shown; it does not explicitly state that there were no effects on gross pathology in this group of animals (data not shown).

# **Overall Quality Determination**

# Medium

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

HERO ID: 1937626 Table: 1 of 1

**Health** Mortality

**Outcome(s):** 

**Reported Health** Mortality

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - rabbits

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
	letric 1: letric 2:	Test Substance Identity Test Substance Source	High High	The test substance was identified definitively as 1,1-dichloroethane.  The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.
M	Ietric 3:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
Domain 2: Test Design				
E	letric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
M	letric 5:	Positive Controls	N/A	Positive controls were not required by study type.
M	letric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Charac M	cterization letric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions
M	letric 8:	Consistency of Exposure Administration	Medium	are not expected to substantially impact the study results.  It appeared that exposures were applied consistently across groups; however, limited details were provided.
M	letric 9:	Reporting of Doses/Concentrations	Low	The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.
M	letric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).
M	fetric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks followed by 13 weeks exposure to 1000 ppm. The concentrations used were not sufficient to elicit a response on any outcome.
M	letric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

Continued on next page ...

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Study Citation: Health	Hofmann, H Mortality	. T., Birnstiel, H., Jobst, P. (1971). On inhala	tion toxicity of	1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.
Outcome(s):				
Reported Health	Mortality			
Effect(s):				
Duration:		(>30-91 days) Up to 6 weeks - rabbits		
Chemical:		bethane- Parent compound		
HERO ID:	1937626			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 1.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended).
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition).
	Metric 17:	Consistency of Outcome Assessment	Low	The time points at which mortality was assessed were not reported.
	Metric 18:	Sampling Adequacy	High	Mortality was presumably monitored in all animals.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Medium	Based on the information reported, it was presumed that no mortality occurred in controls.
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed/not necessary. Based on the information reported, there was no mortality (clearly negative findings across groups).
	Metric 24:	Reporting of Data	Medium	Negative results were reported qualitatively.

# **Overall Quality Determination**

# Medium

Human Health Hazard Animal Toxicology Evaluation

Study Citation:	Milman, H.A	A., Story	, D.L., Ri	ccio, E.S.,	Sivak, A.,	Tu, A.S., Willi	iams, G.	.M., Tong,	C., Tyson,	C.A. (1988).	Rat liver foci and in vitro assays to detect
		_									

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)

Effect(s):

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

Chemical: 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Design				
_	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	Medium	Phenobarbital was used as a positive control for the tumor promotion protocol.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure Ch	aracterization			
-	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure	Low	Gavage volume is not reported for treated animals.
	Mario	Administration	TT' 1	
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	The exposure period (5 days/week for 7 weeks) appears sufficient for determination of tumor promotion potential based on the positive control response.
	Metric 11:	Number of Exposure Groups and	Medium	Only a single dose level was used, but it was justified as the MTD.
		Dose/Concentration Spacing		
	Metric 12:	Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome Ass	sessment			
Domain J. Outcome As.	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment was appropriate and sensitive for tumor promotion potential.
	Metric 17:	Consistency of Outcome Assessment	High	Timing of necropsy was consistent across groups.
	1,100110 17.	Sampling Adequacy	High	Sample size (n = 7-10) was adequate for assessment of tumor promotion potential.

HERO ID: 200479 Table: 1 of 3

#### ... continued from previous page

Study Citation:	Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect
	initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.
Health	Cancer/Carcinogenesis
Outcome(a).	

**Outcome(s):** 

**Reported Health** 

Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)

**Effect(s):** 

Subchronic (>30-91 days) 7 Weeks (promotion protocol) **Duration:** 

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 200479

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology review.
	Metric 20:	Negative Control Response	High	The biological response (incidence of GGT-positive foci) of the negative control group appeared adequate.
Domain 6: Confound	ling / Variable Con	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	There is no evidence of confounding variables in test design and procedures that would affect tumor promotion.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	A low amount of attrition (0-3/10 animals) occurred in this experiment. However, there was no information provided either to support or dismiss the suggestion that differences among groups in health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	High	Incidence data, with standard errors, are reported for each group in Table 4.

# **Overall Quality Determination**

# High

HERO ID: 200479 Table: 2 of 3

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Decreased body weight gain (1,1,2-TCE only)

Effect(s):

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

Chemical: 1,1-Dichloroethane- Parent compound

пекотр:	200479			
Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	N/A	A positive control is not required for the endpoint of body weight.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure	Characterization			
1	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure Administration	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	Animals received the test substance by gavage 5 days/week for 7 weeks, which is appropriate for determining subchronic effects.
	Metric 11:	Number of Exposure Groups and	Medium	Only a single dose level was used, but it was justified as the MTD.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
D : 4 T : 4 :	1			
Domain 4: Test Anim	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was appropriate. Body weight and body weight gain were measured.
	Metric 17:	Consistency of Outcome Assessment	Low	The timing of body weight measurements was not reported.
	Metric 18:	Sampling Adequacy	Low	Sample size for body weight and body weight gain was not reported.
		Contin	ued on next pa	age

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Nutritional/Metabolic

Outcome(s):

**Reported Health** 

Decreased body weight gain (1,1,2-TCE only)

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 200479

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	The outcome (body weight) is not subjective.
	Metric 20:	Negative Control Response	Low	The biological response (body weight) of the negative control group was not reported.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Food and water were provided ad libitum. There is no evidence of confounding variables in test design and procedures that would affect the endpoint of body weight.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	A low amount of attrition (0-3/10 animals) occurred in this experiment. However, there was no information provided either to support or dismiss the suggestion that differences among groups in health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	Low	Results were described only in the text. Numerical values (i.e., body weight, body weight gain) were not provided. The absence of effects on body weight is implied but not explicitly stated.

# **Overall Quality Determination**

# Medium

HERO ID: 200479 Table: 3 of 3

**Study Citation:** Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health

Hepatic/Liver

**Outcome(s): Reported Health** 

Decreased absolute liver weight (1,1,2-TCE only)

Effect(s):

Subchronic (>30-91 days) 7 Weeks (promotion protocol) **Duration:** 

1,1-Dichloroethane- Parent compound **Chemical:** 

HERO ID:	200479			
Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	N/A	A positive control is not required for the endpoint of liver weight.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure	Characterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure Administration	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	Animals received the test substance by gavage 5 days/week for 7 weeks, which is appropriate for determining subchronic effects.
	Metric 11:	Number of Exposure Groups and	Medium	Only a single dose level was used, but it was justified as the MTD.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome	Assessment			
_ J C. Gutcome	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment for liver was very limited (liver weight only).
	Metric 17:	Consistency of Outcome Assessment	High	Timing of necropsy was consistent across groups.
	Metric 18:	Sampling Adequacy	Low	Sample size for liver weight measurements was not reported.
	Metric 19:	Blinding of Assessors	N/A	The outcome (liver weight) is not subjective.
		<del>-</del>	ued on next pa	
		Contin	aca on neat pt	

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 200479 Table: 3 of 3

#### ... continued from previous page

**Study Citation:** Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Hepatic/Liver

**Outcome(s):** 

**Reported Health** Decreased absolute liver weight (1,1,2-TCE only)

Effect(s):

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

**Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 200479

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	Low	The biological response (liver weight) of the negative control group was not reported.
Domain 6: Confound	ling / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Food and water were provided ad libitum. There is no evidence of confounding variables in test design and procedures that would affect the endpoint of liver weight.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	A low amount of attrition (0-3/10 animals) occurred in this experiment. However, there was no information provided either to support or dismiss the suggestion that difference among groups in health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	Low	Results were described only in the text. Numerical values (i.e., absolute and relative liver weights) were not provided. The absence of effects on liver weights is implied bu not explicitly stated.

### **Overall Quality Determination**

### Medium

**Study Citation:** Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. Immune/Hematological; Adrenal; Reproductive/Developmental; Gastrointestinal; Health

**Outcome(s):** 

Reported Health Effect(s):

Immune/Hematological: No effects on histopathology or organ weight of the spleen; Adrenal: Adrenals histopathology were evaluated and no effects were found.; Reproductive/Developmental: No histopathological effects on testis or epididymis; Gastrointestinal: No histopathological effects on the stomach;

HERO ID: 644914 Table: 1 of 6

Subchronic (>30-91 days) 13 weeks **Duration:** Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 644914

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	All Outcomes: Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Immune/Hematological: Reported as 99.99% purity; Adrenal: Reported as 99.99% purity.; Reproductive/Developmental: Reported as 99.99% purity.; Gastrointestinal: Reported as 99.99% purity.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 1.3 mL.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure C	haracterization			
Zomani er Ziposare e	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Nominal dosages were reported, but analytical concentrations were not needed since it was a gavage study.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Doses were administered the test substance once daily for 13 weeks (5 days/week)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The test substance was administered by gavage in corn oil.

Domain 4: Test Animals

Study Citation:	Muralidhara	, S., Ramanathan, R., Mehta, S.M., Lash, I	L.H., Acosta	, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of
·	1,1-dichloro	ethane in rats: Application to risk evaluation	n. Toxicolog	ical Sciences 64(1):135-145.
Health	Immune/Her	natological; Adrenal; Reproductive/Develop	pmental; Ga	strointestinal;
Outcome(s):				
Reported Health	Immune/Her	natological: No effects on histopathology or	r organ weig	tht of the spleen; Adrenal: Adrenals histopathology were evaluated and no effects we
Effect(s):	found.; Repr	oductive/Developmental: No histopatholog	ical effects o	on testis or epididymis; Gastrointestinal: No histopathological effects on the stomach
Duration:	Subchronic (	(>30-91 days) 13 weeks		
Chemical:	1,1-Dichloro	ethane- Parent compound		
HERO ID:	644914			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Sex, strain, and species were reported. In the subchronic study, the rats were male and weighed 180-200 g. The animals were obtained from Harlan (Indianapolis, IN).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: Groups of 15 rats were used in the subchronic study.
D : 5 O :				
Domain 5: Outcome	Assessment Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Organ weight measurement and histopathology were performed.
	Metric 17:		_	
	Metric 17:	Consistency of Outcome Assessment Sampling Adequacy	High Low	All Outcomes: Outcome assessment was consistent for all treatment groups Immune/Hematological: For histopathology, samples were collected from all animals,
	Metric 19:	Blinding of Assessors	High	but it was not reported how many were evaluated per group.; Adrenal: Samples were collected from all animals, but it was not reported how many were evaluated per group.; Reproductive/Developmental: Samples were collected from all animals, but it was not reported how many were evaluated per group.; Gastrointestinal: Samples were collected from all animals, but it was not reported how many were evaluated per group. Immune/Hematological: For histopathology, the study states that tissue specimens were
	Welle 19.	Dilliding of Assessors	mgn	coded and examined in a single-blind fashion by a veterinary pathologist.; Adrenal: The study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.; Reproductive/Developmental: The study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.; Gastrointestinal: The study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.
	Metric 20:	Negative Control Response	High	All Outcomes: No effects were observed in control animals
Domain 6: Confound	ing / Variable Cou	ntrol		
Domain o. Comoulla	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes. The study did not provide sufficient information to determine notantial
		and Procedures		All Outcomes: The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.
	Metric 24:	Reporting of Data	High	All Outcomes: Negative findings were reported qualitatively.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 644914 Table: 1 of 6

#### ... continued from previous page

Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

**Health** Immune/Hematological; Adrenal; Reproductive/Developmental; Gastrointestinal;

**Outcome(s):** 

**Reported Health** Immune/Hematological: No effects on histopathology or organ weight of the spleen; Adrenal: Adrenals histopathology were evaluated and no effects were found.; Reproductive/Developmental: No histopathological effects on testis or epididymis; Gastrointestinal: No histopathological effects on the stomach;

**Duration:** Subchronic (>30-91 days) 13 weeks **Chemical:** 1,1-Dichloroethane- Parent compound

Domain	Metric	Rating	Comments	
Overall Quality Dete	ermination	High		

**Study Citation:** Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health Lung/Respiratory

**Outcome(s):** 

**Reported Health** 

In the acute study, mild focal pneumonitis was "occasionally seen in the lungs of animals, particularly in controls"; pulmonary inflammation was evaluated in the subchronic study and was observed in both control and treated animals.

Effect(s): Subchronic (>30-91 days) 13 weeks **Duration:** 1,1-Dichloroethane- Parent compound **Chemical:** 

Domain		Metric	Rating	Comments
Domain 1: Test Substanc	e			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 1.3 mL.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Cha	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	High	Nominal dosages were reported, but analytical concentrations were not needed since it was a gavage study.
	Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for 13 weeks (5 days/week)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4: Test Animals				
Domain 7. Test Aillildis	Metric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subchronic study, the rats were male and weighed 180-200 g. The animals were obtained from Harlan (Indianapolis, IN).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.
	Metric 15:	Number of Animals per Group	Medium	Groups of 15 rats were used in the subchronic study.

# Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Lung/Respiratory

Outcome(s): Reported Health

In the acute study, mild focal pneumonitis was "occasionally seen in the lungs of animals, particularly in controls"; pulmonary inflammation was evaluated in the subchronic study and was observed in both control and treated animals.

Effect(s):
Duration:
Chemical:
HERO ID:

Subchronic (>30-91 days) 13 weeks 1,1-Dichloroethane- Parent compound

644914

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessmen	ut		
Metri	c 16: Outcome Assessment Methodology	High	Organ weight measurement and histology were performed.
Metri	c 17: Consistency of Outcome Assessment	High	Outcome assessment was consistent for all treatment groups
Metri	c 18: Sampling Adequacy	Medium	Organ weight was measured for all animals. 10/15 Control animals had histology performed, but all treated animals that survived to the end of the treatment period were examined.
Metri	c 19: Blinding of Assessors	High	The study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.
Metri	c 20: Negative Control Response	Medium	2/10 control animals had pulmonary inflammation while treated groups had higher rates of of pulmonary inflammation. The authors describe this as a frequent finding in male rats of this age.
Damain & Canfayndina / Varia	hla Cantual		
Domain 6: Confounding / Varia		3.6.12	
Metri	c 21: Confounding Variables in Test Desig and Procedures	n Medium	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
Metri	c 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Metri	*	High	While the authors do not appear to have performed statistical analysis on pulmonary inflammation, incidence data are provided.
	c 24: Reporting of Data		

Study Citation: Health	1,1-dichloro	, S., Ramanathan, R., Mehta, S.M., Lash, lethane in rats: Application to risk evaluation futritional/Metabolic;		a, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies cical Sciences 64(1):135-145.			
Outcome(s): Reported Health Effect(s):	Mortality: The number of deaths per treatment group.; Nutritional/Metabolic: Reduced body weight gain in subacute and subchronic studies;						
Duration: Chemical: HERO ID:		(>30-91 days) 13 weeks bethane- Parent compound					
Domain		Metric	Rating	Comments			
Domain 1: Test Substanc	ee Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.			
	Metric 2:	Test Substance Source	High	All Outcomes: Test substance was provided by Dow Chemical Co. (Freeport, TX).  Analytical verification was not mentioned, and a batch or lot number were not provided.			
	Metric 3:	Test Substance Purity	High	All Outcomes: Reported as 99.99% purity.			
Domain 2: Test Design							
ooman 20 1000 2001gii	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 1.3 mL.			
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.			
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported that animals were randomly allocated into study groups.			
Domain 3: Exposure Cha	omo otomization						
Domain 3. Exposure Cha	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.			
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.			
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Only nominal dosages were reported.			
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Doses were administered the test substance once daily for 13 weeks (5 days/week)			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.			
	Metric 12:	Exposure Route and Method	High	All Outcomes: The test substance was administered by gavage in corn oil.			
Domain 4: Test Animals							
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Sex, strain, and species were reported. In the subchronic study, the rats were male and weighed 180-200 g. The animals were obtained from Harlan (Indianapolis, IN).			

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Study Citation: Health	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.  Mortality; Nutritional/Metabolic;						
Outcome(s): Reported Health Effect(s):	Mortality: The number of deaths per treatment group.; Nutritional/Metabolic: Reduced body weight gain in subacute and subchronic studies;						
Duration: Chemical: HERO ID:		(>30-91 days) 13 weeks bethane- Parent compound					
Domain		Metric	Rating	Comments			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: Groups of 15 rats were used in the subchronic study.			
Domain 5: Outcome As	ssessment						
	Metric 16:	Outcome Assessment Methodology	High	Mortality: A mortality record was kept.; Nutritional/Metabolic: Body weight was recorded after the administration of the 5th dose each week			
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome assessment was consistent for all treatment groups			
	Metric 18:	Sampling Adequacy	High	Mortality: A mortality record was kept for all animals in the study.; Nutritional/Metabolic: All animals had their body weight measured.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: No blinding was needed.			
	Metric 20:	Negative Control Response	High	Mortality: The control group did not exhibit any mortality; Nutritional/Metabolic: The control group exhibited normal body weight gain.			
Domain 6: Confoundin	g / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Mortality: The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.; Nutritional/Metabolic: The highest dose group was terminated early, but body weight effects were significant up until the 11th week. The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.			
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test.			
	Metric 24:	Reporting of Data	High	Mortality: Findings were reported qualitatively and quantitatively in Figure 3.; Nutritional/Metabolic: Findings were reported qualitatively and quantitatively in Figure 2.			
Overall Quali	ty Detern	nination	High				

Study Citation:		ethane in rats: Application to risk evaluation		a, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of gical Sciences 64(1):135-145.			
Outcome(s): Reported Health Effect(s):	No effect on relative kidney weight or clinical chemistry in acute study; In the subacute study, elevated kidney NSPH was reported after 5 and 10 cthe 2 and 4 g/kg dose groups. In the subchronic study, urinary elimination of ACP and NAG significantly increased at 8 weeks of exposure in the 1						
			ed relative to	o control at 12 weeks, but there was no effect on kidney weight, clinical chemistry,			
D 4	histopatholo						
Duration: Chemical:		(>30-91 days) 13 weeks					
Cnemicai; HERO ID:	644914	oethane- Parent compound					
	044914						
Domain		Metric	Rating	Comments			
Domain 1: Test Substan	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was men-			
	wiedle 1.	Test substance racintry	mgn	tioned.			
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.			
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity.			
Domain 2: Test Design							
	Metric 4:	Negative and Vehicle Controls	High	Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 1.3 mL.			
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.			
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.			
D : 4 E . CI							
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses			
	Metric 7.	Substance	Medium	were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.			
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.			
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only nominal dosages were reported.			
	Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for 13 weeks (5 days/week)			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.			
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.			
D	_						
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subchronic study, the rats were male and weighed 180-200 g. The animals were obtained from Harlan (Indianapolis, IN).			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in pageting flow care rocks in a temperature, and hymidity controlled higherard suite			

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negative flow care racks in a temperature- and humidity-controlled biohazard suite.

Study Citation:	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of
	1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.
Health	Renal/Kidney

Health

**Outcome(s):** 

**Reported Health** Effect(s):

No effect on relative kidney weight or clinical chemistry in acute study; In the subacute study, elevated kidney NSPH was reported after 5 and 10 days in the 2 and 4 g/kg dose groups. In the subchronic study, urinary elimination of ACP and NAG significantly increased at 8 weeks of exposure in the 1, 2 and 4 g/kg exposure groups, and ACP significantly decreased relative to control at 12 weeks, but there was no effect on kidney weight, clinical chemistry, or

histopathology.

**Duration: Chemical:** HERO ID: Subchronic (>30-91 days) 13 weeks 1,1-Dichloroethane- Parent compound

644914

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	Groups of 15 rats were used in the subchronic study.
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Organ weight, histopathology, and clinical chemistry measurements were taken.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent for all treatment groups
	Metric 18:	Sampling Adequacy	Low	Organ weight measurements were taken for all treatment groups, but the number of animals evaluated in each group is not clearly reported. Kidney histopathology was performed on 10/15 control animals, and all treated animals that survived to the end of the treatment period. Urinary indicators NAG and ACP were evaluated for 7-8 rats/treatment group, but sample size for BUN levels is not clearly reported.
	Metric 19:	Blinding of Assessors	High	For histopathology, the study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.
	Metric 20:	Negative Control Response	Low	70% of control animals displayed mild nephropathy, and the treated animals displayed a lower incidence of nephropathy. While this appears to be a common finding in young rats (https://pubmed.ncbi.nlm.nih.gov/21422264/) the effect may reduce the sensitivity of the study to detect kidney effects. Absolute kidney weight was significantly decreased at the two highest dose groups. Urinary excretion of ACP was affected, with a relatively high control value at the end of the treatment period and abnormally low value in the treated groups. No other effects on histopathology, clinical chemistry, or kidney weight were reported.
Domain 6: Confoun	ding / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	A high rate (70%) of mild nephropathy in controls suggest potential for non-chemical effects on health (though this may also just be normal background in young male rats). There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or other health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.
	Metric 24:	Reporting of Data	High	Findings were reported qualitatively and quantitatively in the text and in Table 3, and Figures 4 and 5.

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1,1-Dichloroethane

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Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Renal/Kidney

**Outcome(s):** 

Effect(s):

**Reported Health** 

No effect on relative kidney weight or clinical chemistry in acute study; In the subacute study, elevated kidney NSPH was reported after 5 and 10 days in the 2 and 4 g/kg dose groups. In the subchronic study, urinary elimination of ACP and NAG significantly increased at 8 weeks of exposure in the 1, 2 and

4 g/kg exposure groups, and ACP significantly decreased relative to control at 12 weeks, but there was no effect on kidney weight, clinical chemistry, or

HERO ID: 644914 Table: 4 of 6

histopathology.

**Duration:** Subchronic (>30-91 days) 13 weeks **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 644914

Domain Metric Rating Comments

Overall Quality Determination High

HERO ID: 644914 Table: 5 of 6

**Study Citation:** Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145. Health Hepatic/Liver Outcome(s): Reported Health Decreased absolute and relative liver weight in subacute study; no effects on clinical chemistry in acute or subchronic studies; no effects on liver weight Effect(s): in subchronic study, but authors report a slight difference in hepatocyte histology (mild condensation and a change in cytoplasmic staining consistent with glycogen mobilization) in survivors sacrificed at 11 weeks. **Duration:** Subchronic (>30-91 days) 13 weeks Chemical: 1,1-Dichloroethane- Parent compound HERO ID: 644914 Domain Metric Comments Rating Domain 1: Test Substance Metric 1: Test Substance Identity High The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was men-Metric 2: Test Substance Source High Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided. Metric 3: Test Substance Purity High Reported as 99.99% purity. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High Control animals received 1.0 mL the vehicle (corn oil). The dosage volume for treated animals varied from 0.15 to 1.3 mL. Positive Controls N/A Metric 5: Positive controls are not required for this study type. Metric 6: Randomized Allocation of Animals Medium The study reported that animals were randomly allocated into study groups. Domain 3: Exposure Characterization Preparation and Storage of Test Metric 7: Medium Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorpo-Substance rated into the corn oil, but further methods of preparation were not provided. Consistency of Exposure The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours Metric 8: Low into the rats' light/inactive cycle. Gavage volumes were not consistent for treated an-Administration imals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages. Metric 9: Reporting of Doses/Concentrations Medium Only nominal dosages were reported. Metric 10: Exposure Frequency and Duration High Doses were administered the test substance once daily for 13 weeks (5 days/week) Number of Exposure Groups and Metric 11: Medium The exposure levels were not justified in the paper, but effects were observed at the Dose/Concentration Spacing doses selected and it is unlikely to substantially impact the results. Exposure Route and Method Metric 12: High The test substance was administered by gavage in corn oil. Domain 4: Test Animals Metric 13: **Test Animal Characteristics** High Sex, strain, and species were reported. In the subchronic study, the rats were 180-200 g. The animals were obtained from Harlan (Indianapolis, IN). Metric 14: Adequacy and Consistency of Animal High The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in **Husbandry Conditions** negative flow care racks in a temperature- and humidity-controlled biohazard suite. Metric 15: Number of Animals per Group Medium Groups of 15 rats were used in the subchronic study. Continued on next page ...

#### Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of 1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health

Effect(s):

Hepatic/Liver

Outcome(s): Reported Health

Decreased absolute and relative liver weight in subacute study; no effects on clinical chemistry in acute or subchronic studies; no effects on liver weight in subchronic study, but authors report a slight difference in hepatocyte histology (mild condensation and a change in cytoplasmic staining consistent with

glycogen mobilization) in survivors sacrificed at 11 weeks. Subchronic (>30-91 days) 13 weeks

**Duration:** Subchronic (>30-91 days) 13 weeks **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 644914

Domain		Metric	Rating	Comments
Domain 5: Outcome Asses	ssment			
	Metric 16:	Outcome Assessment Methodology	High	Organ weight, histopathology, clinical chemistry, and cytochrome P450 experiments were performed
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent for all treatment groups
	Metric 18:	Sampling Adequacy	Medium	Organ weight, histopathology, and clinical chemistry measurements were taken. FOr histopathology, samples were collected from all animals, but it was not reported how many were evaluated per group.
	Metric 19:	Blinding of Assessors	High	For histopathology, the study states that tissue specimens were coded and examined in a single-blind fashion by a veterinary pathologist.
	Metric 20:	Negative Control Response	High	No effects were reported in the control group
Domain 6: Confounding /	Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test. LD50 was estimated using Litchfield and Wilcoxon method.
	Metric 24:	Reporting of Data	High	Negative findings on liver weight and mild histopathology findings were reported qualitatively and quantitatively in the text.

# **Overall Quality Determination**

High

Study Citation:	Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of
	1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health Neurological/Behavioral

Outcome(s): Reported Health

CNS depression (excitation followed by progressive motor impairment and sedation) in acute study; No effects on CNS depression or brain weight in the subacute study; Moderate CNS depression and no effects on brain weight or histopathology in the subchronic study.

Effect(s): subacute study; Moderate CNS depress

Duration: Subchronic (>30-91 days) 13 weeks

Chemical: 1,1-Dichloroethane- Parent compound

HERO ID: 644914

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ance			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,1-Dichloroethane (DCE). No CASRN was mentioned.
	Metric 2:	Test Substance Source	High	Test substance was provided by Dow Chemical Co. (Freeport, TX). Analytical verification was not mentioned, and a batch or lot number were not provided.
	Metric 3:	Test Substance Purity	High	Reported as 99.99% purity.
Domain 2: Test Design	n			
Domain 2. Test Besig.	Metric 4:	Negative and Vehicle Controls	High	Control animals received $1.0~\mathrm{mL}$ the vehicle (corn oil). The dosage volume for treated animals varied from $0.15~\mathrm{to}~1.3~\mathrm{mL}$ .
	Metric 5:	Positive Controls	N/A	No positive control was needed.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure (	haracterization			
Bomain 3. Exposure C	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on storage was not provided, but are unlikely to affect the results. The doses were prepared on the day of dosing. The authors stated that the 1,1-DCE was incorporated into the corn oil, but further methods of preparation were not provided.
	Metric 8:	Consistency of Exposure Administration	Low	The authors stated that all dosings occurred between 0900 and 1000 hours; or 3-4 hours into the rats' light/inactive cycle. Gavage volumes were not consistent for treated animals and ranged from 0.15 to 5.1 mL. Chamber designs were consistent. Groups of 4-6 rats were housed together, but some rats were housed individually for 24-hour urine collections in metabolism cages.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only nominal dosages were reported.
	Metric 10:	Exposure Frequency and Duration	High	Doses were administered the test substance once daily for 13 weeks (5 days/week)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The exposure levels were not justified in the paper, but effects were observed at the doses selected and it is unlikely to substantially impact the results.
	Metric 12:	Exposure Route and Method	High	The test substance was administered by gavage in corn oil.
Domain 4: Test Anima	ale			
Domain 7. Test Allille	Metric 13:	Test Animal Characteristics	High	Sex, strain, and species were reported. In the subchronic study, the rats were male and weighed 180-200 g. The animals were obtained from Harlan (Indianapolis, IN).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The authors reported that all animals were acclimated for at least one week to a 12-h light/dark cycle, and were housed together in groups of 4-6 in stainless steel cages in negative flow care racks in a temperature- and humidity-controlled biohazard suite.
	Metric 15:	Number of Animals per Group	Medium	Groups of 15 rats were used in the subchronic study.

#### Continued on next page ...

Study Citation: Muralidhara, S., Ramanathan, R., Mehta, S.M., Lash, L.H., Acosta, D., Bruckner, J.V. (2001). Acute, subacute, and subchronic oral toxicity studies of

1,1-dichloroethane in rats: Application to risk evaluation. Toxicological Sciences 64(1):135-145.

Health Neurological/Behavioral

**Outcome(s):** 

Reported Health Effect(s):

CNS depression (excitation followed by progressive motor impairment and sedation) in acute study; No effects on CNS depression or brain weight in the

HERO ID: 644914 Table: 6 of 6

subacute study; Moderate CNS depression and no effects on brain weight or histopathology in the subchronic study.

**Duration:** Subchronic (>30-91 days) 13 weeks **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 644914

Domain		Metric	Rating	Comments
Domain 5: Outcome Assessi	ment			
M	letric 16:	Outcome Assessment Methodology	Low	Outcome assessment methodology for CNS depression was not described.
M	letric 17:	Consistency of Outcome Assessment	Low	Details regarding outcome assessment protocol were not reported.
M	letric 18:	Sampling Adequacy	Low	Details of sampling for this endpoint were not reported.
M	letric 19:	Blinding of Assessors	Medium	The study did not report whether the assessors were blinded, but lack of blinding is not expected to have a substantial impact on results.
M	letric 20:	Negative Control Response	High	No effects were reported in the control group
Domain 6: Confounding / Va	ariable Con	trol		
M	letric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
M	Ietric 22:	Health Outcomes Unrelated to Exposure	Medium	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
M	Ietric 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA, Keul's test, Duncan's Multiple Range test, but it is not clear whether statistical analysis was performed for CNS depression.
M	letric 24:	Reporting of Data	Low	Findings were reported qualitatively.

# **Overall Quality Determination**

# Medium

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-
	105

Health 107. Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Body weight (6 week and 78 week study), food consumption (78 week study only)

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 6 weeks- Mouse **Chemical:** 1,1-Dichloroethane- Parent compound

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	A negative (corn oil) control group was included.
Metric 5:	Positive Controls	N/A	Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterizatio	n		
Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 6 weeks. Gavage volume and daily timing of test substance administration were not reported.
Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. Analytical/measured doses were not reported.
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and dose spacing were appropriate for the study.
Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, and sex were reported, and the test animals was obtained from a commercial source. Animal age and starting body weight were not reported.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were appropriate.
Metric 15:		Medium	The number of animals was reported (5/sex/group). This is fewer than typically used in a rodent subchronic study, however, is sufficient for this preliminary dose-range finding study.

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weight (6 week and 78 week study), food consumption (78 week study only)

**Effect(s):** 

**Duration:**Subchronic (>30-91 days) 6 weeks- Mouse**Chemical:**1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 5: Outcome Assessn	nent			
Me	etric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest (mean body weights for each group were recorded weekly).
Me	etric 17:	Consistency of Outcome Assessment	Medium	The outcome assessment methodology was incompletely reported (i.e., it is unclear if animal group body weight was determined on the same day each week), however, this is unlikely to have a substantial impact on results.
Me	etric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported.
Me	etric 19:	Blinding of Assessors	N/A	Blinding is not necessary for the outcome being assessed.
Me	etric 20:	Negative Control Response	Low	The biological response (i.e., terminal body weight and weight gain) of the negative control groups were not reported.
Domain 6: Confounding / Va	ariable Con	ntrol		
_	etric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information (i.e., food/water intake was not reported) to determine confounding, but reported information did not identify differences.
Me	etric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Me	etric 23:	Data Presentation and Analysis	N/A	A statistical analysis of body weight data does not appear to have been performed, how- ever, study authors report "no mean body weight depression was observed in mice" so statistical analysis was not necessary.
Me	etric 24:	Reporting of Data	High	Body weight data was not quantitatively reported. However, study authors clearly indicate that no effect on body weight was observed.

# **Overall Quality Determination**

# High

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Mortality; Mortality; Health

**Outcome(s):** 

**Reported Health** 

Mortality: survival; Mortality: survival;

Effect(s):

**Duration:** Subchronic (>30-91 days) 6 weeks- Mouse Chemical: 1,1-Dichloroethane- Parent compound

HERO ID.	040079			
Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	All Outcomes: Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated >99% purity.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A negative (corn oil) control group was included.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	Mortality: The study did not report how animals were allocated to study groups.; Mortality: The study did not report how animals were allocated to study groups,
Domain 3: Exposure Cha				
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Animals were administered test substance 5 days per week for 6 weeks Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Nominal doses were clearly reported in units of mg/kg. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of dose groups and dose spacing were appropriate for the study.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route (oral) and method (gavage) were suited to the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The test animal species, strain, and sex were reported, and the test animals was obtained from a commercial source. Animal age and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported and were appropriate.

### Human Health Hazard Animal Toxicology Evaluation

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**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Mortality; Mortality; Health

**Outcome(s):** 

**Reported Health** 

Mortality: survival; Mortality: survival;

Effect(s):

**Duration:** Subchronic (>30-91 days) 6 weeks- Mouse 1,1-Dichloroethane- Parent compound Chemical:

HERO ID:	646679	edialic Tatent compound		
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals was reported (5/sex/group). This is fewer than typically used in a rodent subchronic study, however, is sufficient for this preliminary dose-range finding study.
Domain 5: Outcom	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Mortality: he outcome assessment methodology addressed the intended outcome of interest.; Mortality: The outcome assessment methodology addressed the intended outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: The outcome assessment methodology was incompletely reported.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Details regarding sampling of outcomes were not reported.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for the outcome being assessed.
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological response of the negative control groups were not reported.
Domain 6: Confour	nding / Variable Co	ntrol		
Bolliani 6. Comour	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information (i.e., food/water intake was not reported) to determine confounding, but reported information did not identify differences.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Uninformative	Mortality: Statistical analysis of mortality data was not performed. Data enabling in- dependent statistical analysis was not provided. Survival data was reported only for the highest treatment group, however, data for other dose levels was not provided and study authors do not explicitly state whether or not any mortality was observed at other dose levels.; Mortality: Statistical analysis of mortality data was not performed. Data enabling independent statistical analysis was not provided. Survival data was provided only for females in the 3160 mg/kg-day group (two animals died), however, data for other dose levels was not provided and study authors do not explicitly state whether or not any mortality was observed at other dose levels.
	Metric 24:	Reporting of Data	Low	Mortality: Data for exposure-related findings were not shown for each study group, but results were partially described in the text. Study authors state "two male and three female mice died at 5620 mg/kg/day," which was the highest dose tested. Study authors do not explicitly state whether or not any mortality was observed at any other dose level.; Mortality: Data for exposure-related findings were not shown for each study group, but results were partially described in the text. Study authors indicate that 2 females in the 3160 mg/kg-day treatment group died Study authors do not explicitly state whether or not any mortality was observed at any other dose level., including whether any females died in the highest treatment group (5620 mg/kg-day).

HERO ID: 646679 Table: 2 of 3

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

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Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

**Health** Mortality; Mortality;

**Outcome(s):** 

**Reported Health** Mortality: survival; Mortality: survival;

Effect(s):

**Duration:** Subchronic (>30-91 days) 6 weeks- Mouse **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain Metric Rating Comments

**Overall Quality Determination** 

Uninformative

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 646679 Table: 3 of 3

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

Nutritional/Metabolic Health

**Outcome(s):** 

Reported Health

Body weight (6 week and 78 week study), food consumption (78 week study only)

Effect(s):

**Duration:** Subchronic (>30-91 days) 6 weeks-rat 1,1-Dichloroethane- Parent compound **Chemical:** 

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Desi	gn			
	Metric 4:	Negative and Vehicle Controls	High	A negative (corn oil) control group was included.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 6 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and dose spacing were appropriate for the study.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.
Domain 4: Test Anir	nals			
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, and sex were reported, and the test animals was obtained from a commercial source. Animal age and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were appropriate.
	Metric 15:	Number of Animals per Group	Medium	The number of animals was reported (5/sex/group). This is fewer than typically used in a rodent subchronic study, however, is sufficient for this preliminary dose-range finding study.

Domain 5: Outcome Assessment

Body weight data is not adequately presented (i.e., group means are variance are not reported), even though some exposure related findings are partially described in text.

enabling an independent statistical analysis were not provided.

		cor	ntinued from previous	page		
Study Citation:		NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-				
Health	107. Nutritional/I	Metabolic				
Outcome(s):						
Reported Health	Body weigh	t (6 week and 78 week study), food consumpti	on (78 week study only	r)		
Effect(s):						
<b>Duration:</b>		(>30-91 days) 6 weeks-rat				
Chemical:	1,1-Dichloro	bethane- Parent compound				
HERO ID:	646679					
Domain		Metric	Rating	Comments		
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest (mean body weights for each group were recorded weekly).		
	Metric 17:	Consistency of Outcome Assessment	Medium	The outcome assessment methodology was incompletely reported (i.e., it is unclear if animal group body weight was determined on the same day each week), however, this is unlikely to have a substantial impact on results.		
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported.		
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for the outcome being assessed.		
	Metric 20:	Negative Control Response	Low	The biological response (i.e., terminal body weight and weight gain) of the negative control groups were not reported.		
Domain 6: Confound	ing / Variable Co	ntrol				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information (i.e., food/water intake was not reported) to determine confounding, but reported information did not identify differences.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.		
	Metric 23:	Data Presentation and Analysis	Uninformative	A statistical analysis of changes in rat body weight data was not performed and data		

# **Overall Quality Determination**

Metric 24:

Reporting of Data

# Uninformative

Uninformative

HERO ID: 1937626 Table: 1 of 10

Study Citation: Health	th Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney;				
Outcome(s): Reported Health Effect(s):  Duration: Chemical:	sulphthalein test (rabbits histology. U serum creati indicating th Chronic (>9 1,1-Dichlore	test (rabbits and cats), liver weight, and liver and cats), liver weight, and liver histology; rine findings evaluated; results not reported	histology; Hep Renal/Kidney: (other than a st	ights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), brompatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney atement indicating that results were "always normal").; Renal/Kidney: BUN and histology. Urine findings evaluated; results not reported (other than a statement	
HERO ID:  Domain	1937626	Metric	Rating	Comments	
Domain 1: Test Substan	ce	Wettic	Kating	Comments	
Domain 1. Test Buesain	Metric 1: Metric 2:	Test Substance Identity Test Substance Source	High High	All Outcomes: The test substance was identified definitively as 1,1-dichloroethane. All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.	
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,1-dichloroethane was about 99%.	
Domain 2: Test Design	Metric 4:  Metric 5:  Metric 6:	Negative and Vehicle Controls  Positive Controls  Randomized Allocation of Animals	High N/A Low	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.  All Outcomes: Positive controls were not required by study type.  All Outcomes: The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Ch					
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.	
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided.	
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.	
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks followed by 13 weeks exposure to 1000 ppm. The concentrations used were not sufficient to elicit a response on any outcome.	
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### Human Health Hazard Animal Toxicology Evaluation

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**Study Citation:** Health Outcome(s):

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney;

Reported Health Effect(s):

Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement

indicating that results were "always normal").;

**Duration:** Chemical: HERO ID: Chronic (>91 days) 26 weeks - rats 1,1-Dichloroethane- Parent compound

1937626

Rating Domain Metric Comments Metric 12: Exposure Route and Method Medium All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

Metric 13: Test Animal Characteristics Medium Nutritional/Metabolic: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 1.; Nutritional/Metabolic: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 2. Note: Based on the context of the study report, data in Figure 2 presumably correspond to rabbits, although this was not explicitly specified.; Hepatic/Liver: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 1.; Hepatic/Liver: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 2. Note: Based on the context of the study report, data in Figure 2 presumably correspond to rabbits, although this was not explicitly specified.; Renal/Kidney: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 1.; Renal/Kidney: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 2. Note: Based on the context of the study report, data in Figure 2 presumably correspond to rabbits, although this was not explicitly specified.

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Study Citation: Health Outcome(s):	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney;  Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;				
Reported Health Effect(s):  Duration:					
Chemical: HERO ID:	•	ethane- Parent compound			
Domain		Metric	Rating	Comments	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).	
	Metric 15:	Number of Animals per Group	Low	Nutritional/Metabolic: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended).; Nutritional/Metabolic: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group would typically be recommended).; Hepatic/Liver: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended).; Hepatic/Liver: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group would typically be recommended).; Renal/Kidney: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended).; Renal/Kidney: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group would typically be recommended).	
Domain 5: Outcome A	Assessment Metric 16:	Outcome Assessment Methodology	High	Nutritional/Metabolic: Based on data presented graphically (see Figure 1), body weights were measured weekly; this was considered appropriate to address the outcome of interest.; Nutritional/Metabolic: Based on data presented graphically (see Figure 2), body weights were measured weekly; this was considered appropriate to address the outcome of interest.; Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: serum ALT and AST, liver weight, and liver histology.; Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: serum ALT and AST, bromsulphthalein test, liver weight, and liver histology.; Renal/Kidney: The outcome assessment addressed the outcome of interest. The following assessments of renal toxicity were performed: BUN, serum creatinine, urinary status (parameters not specified), kidney weight, and kidney histology.; Renal/Kidney: The outcome assessment addressed the outcome of interest. The following assessments of renal toxicity were performed: BUN and serum creatinine, urinary status (parameters not specified), kidney weight, and kidney histology.	
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Study Citation: Health Outcome(s):	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney;			
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), brom-sulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results not reported (other than a statement in			
<b>Duration:</b>		at results were "always normal").; 1 days) 26 weeks - rats		
Chemical: HERO ID:	1,1-Dichloro 1937626	bethane- Parent compound		
Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	High	Nutritional/Metabolic: The results show that body weights were measured for both the group exposed to 1,1-DCA and the controls weekly throughout the experiment.; Nutritional/Metabolic: The results show that body weights were measured for both the group exposed to 1,1-DCA and the controls weekly throughout the experiment.; Hepatic/Liver: The results (Figure 1) show that the activities of liver enzymes were measured for both the group exposed to 1,1-DCA and the controls at the same time points throughout the experiment (the first measurement of AST was not recorded until week 5 in both groups). The text indicates that liver weight and liver histology were assessed in all animals after 26 weeks exposure.; Hepatic/Liver: The results (Figure 2) show that the activities of liver enzymes were measured for both the group exposed to 1,1-DCA and

			sured for both the group exposed to 1,1-DCA and the controls at the same time points throughout the experiment (the first measurement of AST was not recorded until week 5 in both groups). The text indicates that liver weight and liver histology were assessed in all animals after 26 weeks exposure.; Hepatic/Liver: The results (Figure 2) show that the activities of liver enzymes were measured for both the group exposed to 1,1-DCA and the controls at the same time points throughout the experiment (the first measurement of AST was not recorded until week 5 in both groups). The legend to Figure 2 states that the bromsulphthalein test was assessed in exposed animals and controls at the end of the study. The text indicates that liver weight and liver histology were assessed in all animals after 26 weeks exposure.; Renal/Kidney: The results (Figure 1) show that BUN and serum creatinine were measured for both the group exposed to 1,1-DCA and the controls at the same time points throughout the experiment. The text indicates that kidney weight and kidney histology were assessed in all animals after 26 weeks exposure. Urinary status was "repeatedly monitored" during the experimental period.; Renal/Kidney: The results (Figure 2) show that BUN and serum creatinine were measured for both the group exposed to 1,1-DCA and the controls at the same time points throughout the experiment. The text indicates that kidney weight and kidney histology were assessed in all animals after 26 weeks exposure. Urinary status was "repeatedly monitored" during the experiment.
Metric 18:	Sampling Adequacy	High	Nutritional/Metabolic: Body weights were presumably recorded for all animals.; Nutritional/Metabolic: Body weights were presumably recorded for all animals.; Hepatic/Liver: Liver endpoints were assessed in all animals.; Hepatic/Liver: Liver endpoints were presumably assessed in all animals.; Renal/Kidney: Renal endpoints were assessed in all animals.; Renal/Kidney: Renal endpoints were presumably assessed in all animals.
Metric 19:	Blinding of Assessors	N/A	Nutritional/Metabolic: Blinding is not necessary for this outcome.; Nutritional/Metabolic: Blinding is not necessary for this outcome.; Hepatic/Liver: Blinding is not necessary for these outcomes.; Hepatic/Liver: Blinding is not necessary for these outcomes.; Renal/Kidney: Blinding is not necessary for these outcomes.; Renal/Kidney: Blinding is not necessary for these outcomes.

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Study Citation: Health Outcome(s): Reported Health Effect(s):  Duration: Chemical:	Nutritional/Nutrit	Metabolic; Nutritional/Metabolic; Hepatic/Liv Metabolic: Body weights; Nutritional/Metab test (rabbits and cats), liver weight, and liver and cats), liver weight, and liver histology; frine findings evaluated; results not reported nine (rats, rabbits, and cats); kidney weight at results were "always normal").; 11 days) 26 weeks - rats	ver; Hepatic/Livelic: Body wein histology; Hepatic Renal/Kidney: (other than a st	1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. ver; Renal/Kidney; Renal/Kidney;  ights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphtic. Activities of ALT and AST (rats, rabbits, and cats), bromsulphthaleis. BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidnes atement indicating that results were "always normal").; Renal/Kidney: BUN and instology. Urine findings evaluated; results not reported (other than a statement).
Chemical: HERO ID:	1,1-Dichlord 1937626	pethane- Parent compound		
Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	Medium	Nutritional/Metabolic: Control animals gained weight throughout the course of the experiment.; Nutritional/Metabolic: Control animals gained weight throughout the course of the experiment.; Hepatic/Liver: The activities of liver enzymes in controls were shown graphically. The incidence of histopathological lesions in controls was not reported (but presumed to be low).; Hepatic/Liver: The activities of liver enzymes in controls were shown graphically; the percent bromsulphthalein retention in controls was reported in the legend for Figure 2. The incidence of histopathological lesions in controls was not reported (but presumed to be low).; Renal/Kidney: BUN and serum creatinine levels in controls were shown graphically (Figure 1). Urine findings were reportedly normal. The incidence of histopathological lesions in controls was not reporte (but presumed to be low).; Renal/Kidney: BUN and serum creatinine levels in controls were shown graphically (Figure 2). Urine findings were reportedly normal. Although the statement about urine findings was reported in the legend for Figure 1 (rat data), it was presumably applicable to all the laboratory species tested in the study. The incidence of histopathological lesions in controls was not reported (but presumed to be low).
Domain 6: Confoundir	-		3.6 P	
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., I information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.

Study Citation: Health Outcome(s): Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney;

Reported Health Effect(s):

Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), brom-sulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), brom-sulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;

**Duration:** Chronic (>91 days) 26 weeks - rats **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain Metric 23: Data Presentation and Analysis N/A Nutritional/Metabolic: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical manifestations of exposure to 1,1-DCA, including no effects on body weight (clearly negative findings across groups).; Nutritional/Metabolic: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical manifestations of exposure to 1,1-DCA, including no effects on body weight (clearly negative findings across groups).; Hep-

atic/Liver: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical manifestations of exposure to 1,1-DCA, including no effects on liver enzymes, liver weights, or liver histology (clearly negative findings across groups).; Hepatic/Liver: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical manifestations of exposure to 1,1-DCA, including no effects on liver enzymes, bromosulphthalein retention, liver weights, or liver histology (clearly negative findings across groups).; Renal/Kidney: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical manifestations of exposure to 1,1-DCA, including no effects on BUN or serum creatinine, urinary parameters, kidney: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical manifestations of exposure to 1,1-DCA, including no effects on BUN or serum creatinine, urinary status, kidney weights, or kidney histology (clearly negative findings across groups).

Medium

**Study Citation:** Health

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney;

Outcome(s):

Reported Health Effect(s):

Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement

indicating that results were "always normal").;

Chemical: HERO ID:

**Duration:** 

Chronic (>91 days) 26 weeks - rats 1,1-Dichloroethane- Parent compound

1937626

Metric 24:

Rating Domain Metric

Reporting of Data

Comments

HERO ID: 1937626 Table: 1 of 10

Nutritional/Metabolic: Body weight data were reported qualitatively in the text (i.e., there were no clinical manifestations of exposure) and quantitatively in Figure 1. The line graph (Figure 1) includes one continuous line for controls (exposed to 0 ppm for 26 weeks) and one continuous line for 1,1-DCA exposed animals (exposed to 500 ppm for 13 weeks followed by 1000 ppm for 13 weeks). The line for controls goes beyond the upper limit of the graph during weeks 24-26. It would be difficult to determine if there was a biologically significant change (>10%) in body weights based on the graph; however, negative results were reported. Data for males and females were not provided separately.; Nutritional/Metabolic: Body weight data were reported qualitatively in the text (i.e., there were no clinical manifestations of exposure) and quantitatively in Figure 2. The line graph (Figure 2) includes one continuous line for controls (exposed to 0 ppm for 26 weeks) and one continuous line for 1,1-DCA exposed animals (exposed to 500 ppm for 13 weeks followed by 1000 ppm for 13 weeks). The lines go beyond the upper limit of the graph during weeks 24-26. It would be difficult to determine if there was a biologically significant change (>10%) in body weights based on the graph; however, negative results were reported. Data for males and females were not provided separately.; Hepatic/Liver: Data for liver enzymes were reported qualitatively in the text (i.e., there were no clinical manifestations of exposure) and quantitatively in Figure 1. The line graphs for AST and ALT (Figure 1) include one continuous line for controls (exposed to 0 ppm for 26 weeks) and one continuous line for 1,1-DCA exposed animals (exposed to 500 ppm for 13 weeks followed by 1000 ppm for 13 weeks). It would be difficult to determine if there was a biologically significant change (>10%) based on the graphs; however, negative results were reported. The study indicated that histological examination of the livers showed no pathological findings in exposed animals relative to controls, and that relative liver weights showed no "significant" deviations from control animals (it is not clear if significant in this context refers to statistical significance because no statistical methods or results were provided in the study report). Data for males and females were not provided separately.; Hepatic/Liver: Data for liver enzymes and/or bromosulphthalein retention were reported qualitatively in the text (i.e., there were no clinical manifestations of exposure) and quantitatively in Figure 2. The line graphs for AST and ALT (Figure 2) include one continuous line for controls (exposed to 0 ppm for 26 weeks) and one continuous line for 1,1-DCA exposed animals (exposed to 500 ppm for 13 weeks followed by 1000 ppm for 13 weeks). It would be difficult to determine if there was a biologically significant change (>10%) based on the graphs; however, negative results were reported. The study indicated that histological examination of the livers showed no pathological findings in exposed animals relative to controls, and that relative liver weights showed no "significant" deviations from control animals (it is not clear if significant in this context refers to statistical significance because no statistical methods or results were provided in the study report). Data for males and females were not provided separately.; Renal/Kidney: Data for BUN and serum creatinine were reported qualitatively in the text (i.e., there were no clinical manifestations of exposure)

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 1937626 Table: 1 of 10

#### ... continued from previous page

**Study Citation:** Health

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney;

Outcome(s):

Reported Health

Effect(s):

Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein

test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement

indicating that results were "always normal").;

**Duration:** Chemical: Chronic (>91 days) 26 weeks - rats 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain Metric Rating Comments

# **Overall Quality Determination**

### Medium

HERO ID: 1937626 Table: 2 of 10

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Health Hepatic/Liver Outcome(s): Reported Health Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology Effect(s): **Duration:** Chronic (>91 days) 26 weeks - cats Chemical: 1,1-Dichloroethane- Parent compound **HERO ID:** 1937626 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High The test substance was identified definitively as 1,1-dichloroethane. Metric 2: Test Substance Source High The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography. Metric 3: High The purity of 1,1-dichloroethane was about 99%. Test Substance Purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control. Metric 5: Positive Controls N/A Positive controls were not required by study type. Metric 6: Randomized Allocation of Animals Low The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium The study indicated that the test substance (in liquid form) was fed to a steel evaporator Substance by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results. Metric 8: Consistency of Exposure Medium It appeared that exposures were applied consistently across groups; however, limited details were provided. Administration Metric 9: Reporting of Doses/Concentrations The study indicated that the "repeated analytical determination of 1.1-dichloroethane Low in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported. Metric 10: **Exposure Frequency and Duration** High The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations). Metric 11: Number of Exposure Groups and Low The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks Dose/Concentration Spacing followed by 13 weeks exposure to 1000 ppm. Medium Metric 12: Exposure Route and Method The study stated that dynamic air chambers were used without indicating the number of air changes. Domain 4: Test Animals

groups). The legend to Figure 3 states that the bromsulphthalein test was assessed in

Reported information did not identify differences among study groups with respect to

there were no apparent effects on liver enzymes, bromosulphthalein retention, liver

weights, or liver histology (clearly negative findings across groups).

... continued from previous page Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** Health Hepatic/Liver Outcome(s): Reported Health Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology Effect(s): **Duration:** Chronic (>91 days) 26 weeks - cats Chemical: 1,1-Dichloroethane- Parent compound **HERO ID:** 1937626 Domain Metric Rating Comments Test Animal Characteristics Metric 13: Medium The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); Metric 14: Adequacy and Consistency of Animal Low Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum). **Husbandry Conditions** Metric 15: Number of Animals per Group Low The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects. Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology High The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: serum ALT and AST, bromsulphthalein test, liver weight, and liver histology. Metric 17: Consistency of Outcome Assessment High The results (Figure 3) show that the activities of liver enzymes were measured for both the group exposed to 1,1-DCA and the controls at the same time points throughout the experiment (the first measurement of AST was not recorded until week 5 in both

#### exposed animals and controls at the end of the study. The text indicates that liver weight and liver histology were assessed in all animals after 26 weeks exposure. Metric 18: Sampling Adequacy High Liver endpoints were presumably assessed in all animals. N/A Metric 19: Blinding of Assessors Blinding is not necessary for these outcomes. Metric 20: Negative Control Response Medium The activities of liver enzymes in controls were shown graphically; the percent bromsulphthalein retention in controls was reported in the legend for Figure 3. The incidence of histopathological lesions in controls was not reported (but presumed to be low).

#### Domain 6: Confounding / Variable Control

Metric 21:

Confounding Variables in Test Design

Medic 21.	and Procedures	172GIGHT	confounding factors; however, limited information was provided (e.g., no information on respiration rates).
Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The study reported that there was an "intercurrent catarrhal infection" that contributed to body weight loss starting in week 11. The degree and extent of infection and the number of affected animals were not reported. It was not possible to differentiate between effects that were due to 1,1-DCA exposure and those that may have been caused by infection.
Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed/not necessary. Based on the information reported,

#### Continued on next page ...

Medium

HERO ID: 1937626 Table: 2 of 10

1,1-Dichloroethane

### ... continued from previous page

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

h Hepatic/Liver

**Outcome(s):** 

Reported Health

Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - cats **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Medium	Results were reported qualitatively in the text (e.g., for bromsulphthalein retention in the legend for Figure 3) and quantitatively (liver enzymes in Figure 3). The line graph (Figure 3) shows one continuous line for controls (exposed to 0 ppm for 26 weeks) and one continuous line for 1,1-DCA exposed animals (exposed to 500 ppm for 13 weeks followed by 1000 ppm for 13 weeks). Data for males and females were not provided separately. The data for cats also presumably included one cat (sex not specified) that was taken out of the experiment prematurely owing to poor general condition after 23 weeks and cats (both groups) with infection. The study implied, but did not explicitly state, that there were no effects on relative liver weight or liver histology.

# **Overall Quality Determination**

# Uninformative

HERO ID: 1937626 Table: 3 of 10

Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weights

**Effect(s):** 

**Duration:** Chronic (>91 days) 26 weeks - cats **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as 1,1-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.
	Metric 3:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	Characterization			
·	Metric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporato by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Give that the test substance was analytically verified in the inhalation chamber, any omission are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Low	The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 week followed by 13 weeks exposure to 1000 ppm.
	Metric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Outcome(s):

Reported Health

Body weights

Nutritional/Metabolic

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - cats **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

HERO ID:	1937020			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 3.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Based on data presented graphically (see Figure 3), body weights were measured weekly; this was considered appropriate to address the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The results show that body weights were measured for both the group exposed to 1,1-DCA and the controls weekly throughout the experiment.
	Metric 18:	Sampling Adequacy	High	Body weights were presumably recorded for all animals.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Medium	Control animals generally gained weight over the course of the experiment; however, body weight loss occurred at week 11. The study authors indicated that this body weigh loss was due to intercurrent infection.
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information or respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The study reported that there was an "intercurrent catarrhal infection" that contributed to body weight loss starting in week 11. The degree and extent of infection and the number of affected animals were not reported. It was not possible to differentiate between effects that were due to 1,1-DCA exposure and those that may have been caused by infection.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed/not necessary (biological significance can be assessed as a >10% change in body weights from controls).

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

HERO ID: 1937626 Table: 3 of 10

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weights

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - cats 1,1-Dichloroethane- Parent compound Chemical:

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Uninformative	Results were reported qualitatively in the text (i.e., "after increasing the concentration
				to 1000 ppm, body weight gain was delayed or stopped") and quantitatively (Figure
				3). The line graph (Figure 3) shows one continuous line for controls (exposed to 0 ppr
				for 26 weeks) and one continuous line for 1,1-DCA exposed animals (exposed to 500
				ppm for 13 weeks followed by 1000 ppm for 13 weeks). Although an effect on body
				weight was reported, it would be difficult to determine when there was a biologically
				significant change (>10%) based on the data provided. Data for males and females
				were not provided separately. The data for cats also presumably included one cat (sex
				not specified) that was taken out of the experiment prematurely owing to poor genera
				condition after 23 weeks and cats (in both groups) with infection.

# **Overall Quality Determination**

# Uninformative

HERO ID: 1937626 Table: 4 of 10

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** Health Renal/Kidney Outcome(s): Reported Health BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal"). Effect(s): **Duration:** Chronic (>91 days) 26 weeks - cats Chemical: 1,1-Dichloroethane- Parent compound **HERO ID:** 1937626 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High The test substance was identified definitively as 1,1-dichloroethane. Metric 2: Test Substance Source High The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography. Metric 3: High The purity of 1,1-dichloroethane was about 99%. Test Substance Purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control. Metric 5: Positive Controls N/A Positive controls were not required by study type. Metric 6: Randomized Allocation of Animals Low The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium The study indicated that the test substance (in liquid form) was fed to a steel evaporator Substance by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results. Metric 8: Consistency of Exposure Medium It appeared that exposures were applied consistently across groups; however, limited details were provided. Administration Metric 9: Reporting of Doses/Concentrations Low The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported. Metric 10: **Exposure Frequency and Duration** High The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations). Metric 11: Number of Exposure Groups and Low The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks Dose/Concentration Spacing followed by 13 weeks exposure to 1000 ppm. Medium Metric 12: Exposure Route and Method The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Renal/Kidney

Health

**Outcome(s):** 

Reported Health

BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a

Effect(s): **Duration:**  statement indicating that results were "always normal"). Chronic (>91 days) 26 weeks - cats

Chemical: **HERO ID:**  1,1-Dichloroethane- Parent compound

1937626

Domain	Metric	Rating	Comments
Metric 13:	Test Animal Characteristics	Medium	The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 3.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
Metric 15:	Number of Animals per Group	Low	The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment addressed the outcome of interest. The following assessments of renal toxicity were performed: creatinine, urinary status (parameters not specified), kidney weight, and kidney histology.
Metric 17:	Consistency of Outcome Assessment	High	The results (Figure 3) show that BUN and serum creatinine were measured for both the group exposed to 1,1-DCA and the controls at the same time points throughout the experiment. The text indicates that kidney weight and kidney histology were assessed in all animals after 26 weeks exposure. Urinary status was "repeatedly monitored" during the experimental period.
Metric 18:	Sampling Adequacy	High	Renal endpoints were presumably assessed in all animals.
Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for these outcomes.
Metric 20:	Negative Control Response	Medium	BUN and serum creatinine levels in controls were shown graphically (Figure 3). Urine findings in controls were reportedly normal. Although the statement about urine findings was reported in the legend for Figure 1 (rat data), it was presumably applicable to all the laboratory species tested in the study. The incidence of histopathological lesions in controls was not reported (but presumed to be low).
Domain 6: Confounding / Variable Co	ntrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The study reported that there was an "intercurrent catarrhal infection" that contributed to body weight loss starting in week 11. The degree and extent of infection and the number of affected animals were not reported. It was not possible to differentiate between effects that were due to 1,1-DCA exposure and those that may have been caused by infection.
Metric 23:	Data Presentation and Analysis	Uninformative	Statistical analysis was not performed and data were not provided for independent anal-

HERO ID: 1937626 Table: 4 of 10

1,1-Dichloroethane

#### ... continued from previous page

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a

Effect(s):

statement indicating that results were "always normal").

**Duration:** Chemical:

Chronic (>91 days) 26 weeks - cats 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

HERO ID:	1937020			
Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Uninformative	Results were reported qualitatively in the text (e.g., increased BUN and serum creatinine) and quantitatively (Figure 3). The line graphs for BUN and creatinine (Figure 3) show one continuous line for controls (exposed to 0 ppm for 26 weeks) and one continuous line for 1,1-DCA exposed animals (exposed to 500 ppm for 13 weeks followed by 1000 ppm for 13 weeks). Data for males and females were not provided separately. The data for cats also presumably included one cat (sex not specified) that was taken out of the experiment prematurely owing to poor general condition after 23 weeks (the text noted that increases in BUN and creatinine were due in large part to this animal) and cats (both groups) with infection. Urine findings were reportedly "normal" in exposed cats and controls. Histological kidney findings (e.g., renal tubule dilatation), which were reported in 3 of 4 cats, were described in the text (number of controls with histological effects was not explicitly specified). Although effects on clinical pathology related to kidney function and kidney histology were reported, missing/unclear information makes these data difficult to interpret.

# **Overall Quality Determination**

### Uninformative

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Mortality; Mortality;

**Outcome(s):** 

**Reported Health** 

Mortality: Mortality; Mortality; Mortality;

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - rabbits **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain		Metric	Rating	Comments	
Domain 1: Test Substan	nce				
	Metric 1: Metric 2:	Test Substance Identity Test Substance Source	High High	All Outcomes: The test substance was identified definitively as 1,1-dichloroethane.  All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.	
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,1-dichloroethane was about 99%.	
Domain 2: Test Design					
C	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.	
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.	
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.	
Domain 3: Exposure C	haracterization Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.	
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided.	
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.	
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks followed by 13 weeks exposure to 1000 ppm. The concentrations used were not sufficient to elicit a response on any outcome.	
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.	

Domain 4: Test Animals

HERO ID: 1937626 Table: 5 of 10

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Mortality; Mortality;

Health

**Outcome(s):** 

**Reported Health** 

Mortality: Mortality; Mortality; Mortality;

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - rabbits 1,1-Dichloroethane- Parent compound **Chemical:** 

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	Mortality: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 2. Note: Based on the context of the study report, data in Figure 2 presumably correspond to rabbits, although this was not explicitly specified.; Mortality: The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
		Number of Animals per Group	Low	Mortality: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group would typically be recommended).; Mortality: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition).
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: The time points at which mortality was assessed were not reported.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Mortality was presumably monitored in all animals.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Medium	All Outcomes: Based on the information reported, it was presumed that no mortality occurred in controls.
Domain 6: Confound	ling / Variable Co	ntrol		
Domain o. Comount	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not performed/not necessary. Based on the information reported, there was no mortality (clearly negative findings across groups).
	Metric 24:	Reporting of Data	Medium	All Outcomes: Negative results were reported qualitatively.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 1937626 Table: 5 of 10

### ... continued from previous page

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Mortality; Mortality;

**Outcome(s):** 

Reported Health

Mortality: Mortality; Mortality; Mortality;

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - rabbits 1,1-Dichloroethane- Parent compound Chemical:

**HERO ID:** 1937626

Domain Metric Rating Comments

**Overall Quality Determination** Medium Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

HERO ID: 1937626 Table: 6 of 10

Health

Mortality

**Outcome(s):** 

**Study Citation:** 

Reported Health

Mortality

Effect(s): Duration:

Chemical:

Chronic (>91 days) 26 weeks - cats 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ince			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as 1,1-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.
	Metric 3:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	Characterization			
·	Metric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Low	The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks followed by 13 weeks exposure to 1000 ppm.
	Metric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

HERO ID: 1937626 Table: 6 of 10

### ... continued from previous page

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

**Outcome(s):** 

**Reported Health** 

.

Mortality

Mortality

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - cats **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

HERO ID:	1937020			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 3.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition).
	Metric 17:	Consistency of Outcome Assessment	Low	The time points at which mortality was assessed were not reported.
	Metric 18:	Sampling Adequacy	High	Mortality was presumably monitored in all animals.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Medium	Based on the information reported, it was presumed that no mortality occurred in controls.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The study reported that there was an "intercurrent catarrhal infection" that contributed to body weight loss starting in week 11. The degree and extent of infection and the number of affected animals were not reported. It was not possible to differentiate between effects that were due to 1,1-DCA exposure and those that may have been caused by infection.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed/not necessary. Based on the information reported, there was no mortality. One exposed cat (sex not specified) was removed from the study after 23 weeks owing to poor general condition; however, this cat presumably did not die/was not sacrificed moribund because pathological data were reported for this cat during the non-experimental period.
	Metric 24:	Reporting of Data	Medium	Results were reported qualitatively.

# **Overall Quality Determination**

# Uninformative

HERO ID: 1937626 Table: 7 of 10

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights

**Effect(s):** 

**Duration:** Chronic (>91 days) 26 weeks - guinea pigs 1,1-Dichloroethane- Parent compound Chemical:

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as 1,1-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.
	Metric 3:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
Domain 2: Test Design	l			
C	Metric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Low	The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks followed by 13 weeks exposure to 1000 ppm. The concentrations used were not sufficient to elicit a response on any outcome.
	Metric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights

**Effect(s):** 

**Duration:** Chronic (>91 days) 26 weeks - guinea pigs **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

HERO ID.	1737020			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Mortality was presumably measured appropriately (i.e., regular body weight measurements).
	Metric 17:	Consistency of Outcome Assessment	Medium	The time points at which body weights were recorded was not specified in the methods. Based on information for other species included in the same study (rats, rabbits, and cats), body weights were probably recorded weekly.
	Metric 18:	Sampling Adequacy	High	Body weights were presumably recorded for all animals.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Low	Body weight information for the control group was not reported.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information or respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed/not necessary. Based on the information reported "the weight development of the guinea pigs also showed no deviations compared to the control animals" (clearly negative findings across groups).
	Metric 24:	Reporting of Data	Medium	Negative results were reported qualitatively (quantitative body weight data were not provided).

# **Overall Quality Determination**

# Medium

HERO ID: 1937626 Table: 8 of 10

Health Outcome(s):	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Hepatic/Liver; Renal/Kidney;					
Reported Health Effect(s):	Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a					
Duration: Chemical: HERO ID:	statement indicating that results were "always normal").; Chronic (>91 days) 26 weeks - guinea pigs 1,1-Dichloroethane- Parent compound 1937626					
Domain		Metric	Rating	Comments		
Domain 1: Test Substance						
	Metric 1: Metric 2:	Test Substance Identity Test Substance Source	High High	All Outcomes: The test substance was identified definitively as 1,1-dichloroethane. All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.		
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,1-dichloroethane was about 99%.		
Domain 2: Test Design						
Bonium 2. Test Besign	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.		
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.		
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.		
Domain 3: Exposure Cha	racterization					
Domain 3. Exposure Cha	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.		
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; how- ever, limited details were provided.		
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.		
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).		
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppn for 13 weeks followed by 13 weeks exposure to 1000 ppm. The concentrations used were not sufficient to elicit a response on any outcome.		
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.		

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Study Citation: Health			tion toxicity of	1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.		
Outcome(s):	Hepatic/Liver; Renal/Kidney;					
Reported Health	Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney:					
Effect(s):	BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a					
•		dicating that results were "always normal").;	, ,			
<b>Duration:</b>		11 days) 26 weeks - guinea pigs				
Chemical:	1,1-Dichloroethane- Parent compound					
HERO ID:	1937626					
Domain		Metric	Rating	Comments		
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).		
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).		
Domain 5: Outcome A	ssessment					
	Metric 16:	Outcome Assessment Methodology	Medium	Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: liver weight and liver histology. Clinical pathological measurements of liver function (e.g., liver enzymes) were not done.; Renal/Kidney: The outcome assessment addressed the outcome of interest. The following assessments of renal toxicity were performed: kidney weight and kidney histology. Clinical pathological measurements of kidney function (e.g., BUN or serum creatinine) were not done.		
	Metric 17:	Consistency of Outcome Assessment	High	Hepatic/Liver: The text indicates that liver weight and liver histology were assessed in all animals after 26 weeks exposure.; Renal/Kidney: The text indicates that kidney weight and kidney histology were assessed in all animals after 26 weeks exposure.		
	Metric 18:	Sampling Adequacy	High	Hepatic/Liver: Liver endpoints were presumably assessed in all animals.; Renal/Kidney: Renal endpoints were presumably assessed in all animals.		
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for these outcomes.		
	Metric 20:	Negative Control Response	Medium	All Outcomes: The incidence of histopathological lesions in controls was not reported (but presumed to be low).		
Domain 6: Confoundin	ng / Variable Co	ntrol				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.		
	Metric 23:	Data Presentation and Analysis	N/A	Hepatic/Liver: Statistical analysis was not performed/not necessary. Based on the information reported, there were no effects on relative liver weights or liver histology (clearly negative findings across groups).; Renal/Kidney: Statistical analysis was not performed/not necessary. Based on the information reported, there were no effects on relative kidney weights or kidney histology (clearly negative findings across groups).		

HERO ID: 1937626 Table: 8 of 10

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**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Effect(s):

Hepatic/Liver; Renal/Kidney;

Outcome(s): Reported Health

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney:

BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a

statement indicating that results were "always normal").;

**Duration: Chemical:**  Chronic (>91 days) 26 weeks - guinea pigs 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Medium	Hepatic/Liver: Negative results were reported qualitatively. The study indicated that histological examination of the livers showed no pathological findings in exposed animals relative to controls, and that relative liver weights showed no "significant" deviations from control animals (it is not clear if significant in this context refers to statistical significance because no statistical methods or results were provided in the study report). Data for males and females were not provided separately.; Renal/Kidney: Negative results were reported qualitatively. The study indicated that histological examination of the kidneys showed no pathological findings in exposed animals relative to controls, and that relative kidney weights showed no "significant" deviations from control animals (it is not clear if significant in this context refers to statistical significance because no statistical methods or results were provided in the study report). Data for males and females were not provided separately.

# **Overall Quality Determination**

### Medium

HERO ID: 1937626 Table: 9 of 10

Study Citation: Health	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Immune/Hematological; Immune/Hematological;				
Outcome(s):					
Reported Health	Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific				
Effect(s):	parameters not specified (rats, rabbits, and cats only);				
Duration:	Chronic (>91 days) 26 weeks - rats				
Chemical:		bethane- Parent compound			
HERO ID:	1937626				
Domain		Metric	Rating	Comments	
Domain 1: Test Substan					
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,1-dichloroethane.	
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.	
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,1-dichloroethane was about 99%.	
Domain 2: Test Design					
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.	
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.	
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.	
Domain 2. Evmagues Ch					
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.	
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided.	
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.	
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks followed by 13 weeks exposure to 1000 ppm. The concentrations used were not sufficient to elicit a response on any outcome.	
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.	
Domain 4: Test Animals	8	Contra	uod on		
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**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health Immune/Hematological; Immune/Hematological;

**Outcome(s):** 

Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific Reported Health

Effect(s): parameters not specified (rats, rabbits, and cats only);

Chronic (>91 days) 26 weeks - rats **Duration:** Chemical: 1,1-Dichloroethane- Parent compound HEDO ID

	1937626			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	Immune/Hematological: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 1.; Immune/Hematological: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 2. Note: Based on the context of the study report, data in Figure 2 presumably correspond to rabbits, although this was not explicitly specified.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	Immune/Hematological: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended).; Immune/Hematological: The study used fewer animals pe group than would be recommended for studies of this type (i.e., there were 2 rabbits/sex when at least 5/sex/group would typically be recommended).
Domain 5: Outcome	Assessment			
Domain 5. Outcome	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The study indicated that blood counts (parameters not specified) were repeatedly monitored during the experimental period.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: The time points at which blood counts were measured in controls and 1,1-DCA exposed animals was not reported.
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	Metric 18:	Sampling Adequacy	High	All Outcomes: Blood counts were presumably measured in all animals.
	Metric 18: Metric 19:	Sampling Adequacy Blinding of Assessors	High N/A	All Outcomes: Blood counts were presumably measured in all animals.  All Outcomes: Blinding is not necessary for this outcome.
			_	
Domain 6: Confound	Metric 19: Metric 20:	Blinding of Assessors Negative Control Response	N/A	All Outcomes: Blinding is not necessary for this outcome.  Immune/Hematological: The study authors indicated that results for controls were normal.; Immune/Hematological: The study authors indicated that results for controls were normal. This statement was indicated in the legend for Figure 1 (rat data) but appeared
Domain 6: Confound	Metric 19: Metric 20:	Blinding of Assessors Negative Control Response	N/A	All Outcomes: Blinding is not necessary for this outcome.  Immune/Hematological: The study authors indicated that results for controls were normal.; Immune/Hematological: The study authors indicated that results for controls were normal. This statement was indicated in the legend for Figure 1 (rat data) but appeared

Study Citation: Health Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Immune/Hematological; Immune/Hematological;

**Outcome(s):** 

Reported Health

Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific

**Effect(s):** parameters not specified (rats, rabbits, and cats only);

**Duration:** Chronic (>91 days) 26 weeks - rats **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	N/A	Immune/Hematological: Statistical analysis was not performed/not necessary. The study reported that blood counts were "always normal" (clearly negative findings across groups).; Immune/Hematological: Statistical analysis was not performed/not necessary. The study reported that blood counts were "always normal" (clearly negative findings across groups). The statement that blood counts were normal was indicated in the legend for Figure 1 (rat data) but appeared to be applicable to all the laboratory species tested in the study.
	Metric 24:	Reporting of Data	Medium	Immune/Hematological: Negative results were reported qualitatively. The study indicated that there were no "clinically or chemically detectable changes" compared to controls and that blood counts were "always normal."; Immune/Hematological: Negative results were reported qualitatively. The study indicated that there were no "clinically or chemically detectable changes" compared to controls.

# **Overall Quality Determination**

# Medium

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 1937626 Table: 10 of 10

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

**Outcome(s):** 

Reported Health

Blood counts - specific parameters not specified (rats, rabbits, and cats only)

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - cats 1,1-Dichloroethane- Parent compound Chemical:

Immune/Hematological

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as 1,1-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance source was reported as "Dr. Schuchardt GmbH" (i.e., it is not clear that the test substance was obtained from a commercial source); however, the test substance was analytically verified using gas chromatography.
	Metric 3:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Characterization			
·	Metric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Low	The study indicated that the "repeated analytical determination of 1.1-dichloroethane in the inhalation chamber was carried out by gas chromatography," but the analytical concentration associated with the 500 ppm exposure was not reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 13 weeks each at two different exposure concentrations).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The study only evaluated exposure to 1,1-DCA at one concentration at a time (i.e., one exposure group plus the control group); animals were exposed to 500 ppm for 13 weeks followed by 13 weeks exposure to 1000 ppm.
	Metric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Immune/Hematological

Health

**Outcome(s):** 

Reported Health

Blood counts - specific parameters not specified (rats, rabbits, and cats only)

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - cats 1,1-Dichloroethane- Parent compound **Chemical:** 

HERO ID:	1937626	^		
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were only shown graphically (combined data for males and females); see Figure 3.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.
Domain 5: Outcome Asse	essment			
	Metric 16:	Outcome Assessment Methodology	Medium	The study indicated that blood counts (parameters not specified) were repeatedly monitored during the experimental period.
	Metric 17:	Consistency of Outcome Assessment	Low	The time points at which blood counts were measured in controls and 1,1-DCA exposed animals was not reported.
	Metric 18:	Sampling Adequacy	High	Blood counts were presumably measured in all animals.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Medium	The study authors indicated that results for controls were normal. This statement was indicated in the legend for Figure 1 (rat data) but appeared to be applicable to all the laboratory species tested in the study.
Domain 6: Confounding /	' Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The study reported that there was an "intercurrent catarrhal infection" that contributed to body weight loss starting in week 11. The degree and extent of infection and the number of affected animals were not reported. It was not possible to differentiate between effects that were due to 1,1-DCA exposure and those that may have been caused by infection.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed/not necessary. The study reported that blood counts were "always normal" (clearly negative findings across groups). The statement that blood counts were normal was indicated in the legend for Figure 1 (rat data) but appeared to be applicable to all the laboratory species tested in the study.
	Metric 24:	Reporting of Data	Medium	Negative results were reported qualitatively. The results may have included data for one cat (sex not specified) that was removed from the experiment prematurely owing to poor general condition after 23 weeks and cats (both groups) with infection.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

HERO ID: 1937626 Table: 10 of 10

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Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** 

Health

Immune/Hematological

**Outcome(s):** 

Blood counts - specific parameters not specified (rats, rabbits, and cats only) Reported Health

Effect(s):

**Duration:** Chronic (>91 days) 26 weeks - cats Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 1937626

Domain Metric Rating Comments

# **Overall Quality Determination**

# Uninformative

HERO ID: 200427 Table: 1 of 4

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Cancer/Carcinogenesis Health

**Outcome(s):** 

**Reported Health** Tumor incidence

Effect(s):

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Tumor promotion

1,1-Dichloroethane- Parent compound Chemical:

Domain		Metric	Rating	Comments
Domain 1: Test Substan	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Design	l			
· ·	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only, and initiator (DENA) only
	Metric 5:	Positive Controls	Low	PB was included as a positive control for liver tumor formation; the text reports that a significant increase in incidence was observed, it is unclear how this significance was determined as it appears to be incorrect. Incidences at 24 wks were: 7/10 initiated only controls, vs 9/10 those treated with PB, which does not reach significance based on independent review. However, the number of tumors/mouse was significantly increased over controls, and therefore the test was considered valid.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure C		D C LC CT	TT: 1	
	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflon stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
		Administration		
	Metric 9:	Reporting of Doses/Concentrations	High	The doses were reported as mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group, the study Authors did report an Approximate weekly dose mg/kg body weight, however, the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were exposed continuously in drinking water for up to 52 weeks. This duration is shorter than is acceptable for a standard cancer study in mice (>= 18 months would be considered appropriate for mice). However, this study also tested the potential for tumor promotion, and the study duration was considered acceptable for this purpose.
		C	ontinued on next nage	

HERO ID: 200427 Table: 1 of 4

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** 

Tumor incidence

Effect(s):

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Tumor promotion **Duration:** 

1,1-Dichloroethane- Parent compound **Chemical:** 

HERO ID:	200427			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Dose levels were based on preliminary studies and were justified by the study authors. Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three dose levels for a carcinogenicity study
	Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.
Domain 4: Test Anima	a <b>l</b> e			
Domain 4. Test Ammi	Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group (35 males only/group) was lower than the typical number used in a standard cancer bioassay, but may be appropriate for a short-duration tumor promotion assay
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Appropriate standard techniques were described for this outcome of interest, although minimal details were provided (e.g., number of samples/tissue, number of slides examined etc.,)
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
	Metric 18:	Sampling Adequacy	Medium	10 animals/sex/group were sampled at 24 weeks, leaving 25 animals/sex/group at the 52 week evaluation. It is unclear if sampling was appropriate since no effects were observed.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
	Metric 20:	Negative Control Response	Uninformative	The response of the tumor initiator only control group was too strong (72-100% of animals had tumors at 52 weeks), and this precluded the ability to determine whether the test substance could function as a tumor promoter.
Domain 6: Confoundi	ng / Variable Co	ntrol		
s. comound	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Drinking water intake was graphically reported for the experimental, and control groups (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text discusses significant differences in drinking water intake results for other chemicals but does not report results for the COI.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.

HERO ID: 200427 Table: 1 of 4

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Cancer/Carcinogenesis

**Outcome(s):** 

Reported Health

Effect(s):

Tumor incidence

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Tumor promotion

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 200427

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was clearly performed for some endpoints (text reports whether results were significant or not); however, the type of analysis (methods) used are not described.
	Metric 24:	Reporting of Data	High	Tumor incidence data was well documented.

# **Overall Quality Determination**

## Uninformative

HERO ID: 200427 Table: 2 of 4

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice. Environmental Health Perspectives 69:89-95. Cancer/Carcinogenesis Health

**Outcome(s):** 

**Reported Health** 

Tumor incidence

Effect(s):

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay **Duration:** 

Chemical: 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only
	Metric 5:	Positive Controls	Low	A positive control is generally not required for a cancer bioassay, but a PB control for liver tumor formation was included. The text indicates PB produced significant responses at both collection points, however, independent analysis did not find either the incidence at 24 weeks (2/10 vs. 0/10 in controls), or at 52 weeks (9/25 vs. 5/25) to reac statistical significance (Fisher's exact). The only significant positive response appears to be an increase in the number of tumrps/mouse at 52 weeks. Overall, the positive control (in combination with a poor study design) did not appear to adequately show the study was sensitive to detect tumor promotion ability.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure Ch				
	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflor stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
	Metric 9:  Metric 10:	Administration Reporting of Doses/Concentrations  Exposure Frequency and Duration	High Uninformative	The doses were reported in mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group the study Authors did report an Approximate weekly dose mg/kg body weight, however the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.  Animals were exposed continuously via drinking water for up to 52 weeks. This du-
		1 1 3		ration is shorter than is acceptable for a standard cancer study in mice (>= 18 months would be considered appropriate for mice) and is inadequate for determining tumorigenicity.

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** 

Tumor incidence

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

Chemical: 1,1-Dichloroethane- Parent compound

HERO ID:	200427			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Dose levels were based on preliminary studies and were justified by the study authors.  Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three dose levels for a carcinogenicity study
	Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.
Domain 4: Test Animal	S			
201111111111111111111111111111111111111	Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
	Metric 15:	Number of Animals per Group	Low	The number of animals/group (35 males only/group) was lower than the typical number used in studies of the same or similar type.
Domain 5: Outcome As	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	Appropriate standard techniques were described for this outcome of interest, although minimal details were provided (e.g., number of samples/tissue, number of slides examined etc.,)
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
	Metric 18:	Sampling Adequacy	Medium	10 animals/sex/group were sampled at 24 weeks, leaving 25 animals/sex/group at the 52-week evaluation. It is unclear if sampling was appropriate since no effects were observed.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
	Metric 20:	Negative Control Response	High	The negative untreated (water only) control group appeared to have an appropriate response.
Domain 6: Confounding	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Drinking water intake was graphically reported for the experimental, and control groups (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text discusses significant differences in drinking water intake results for other chemicals but does not report results for the COI.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.

HERO ID: 200427 Table: 2 of 4

### ... continued from previous page

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** Tumor incidence

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 200427

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was clearly performed for some endpoints (text reports whether results were significant or not); however, the type of analysis (methods) used are not described.
	Metric 24:	Reporting of Data	High	Tumor incidence data was well documented.

# Overall Quality Determination Uninformative

HERO ID: 200427 Table: 3 of 4

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights; water intake

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 200427

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only
	Metric 5:	Positive Controls	N/A	A positive control is generally not required for this endpoint
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure C	haracterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflon stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
	Metric 9:	Administration Reporting of Doses/Concentrations	High	The doses were reported in mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group, the study Authors did report an Approximate weekly dose mg/kg body weight, however, the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously via drinking water for up to 52 weeks. This is acceptable for the endpoint(s) of interest
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Dose levels were based on preliminary studies and were justified by the study authors. Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three-dose levels for a carcinogenicity study, but appropriate for the endpoint of interest.
	Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.

Domain 4: Test Animals

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice. Environmental Health Perspectives 69:89-95.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights; water intake

Effect(s):

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay **Duration:** 1,1-Dichloroethane- Parent compound

Chemical:

HERO ID:	200427			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
	Metric 15:	Number of Animals per Group	Low	The number of animals/group (35 males only/group) was lower than the typical number used in a chronic study, and typically both sexes are preferred.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Body weights were only recorded monthly and on a per-cage basis. The study does not specify how many mice were per cage. This is not a standard practice for body weight measurements. Drinking water consumption was measured weekly. The mean water intake (in grams) of each mouse per day was calculated by subtracting the weight of water after 1 week from the weight of the water at time of filing and dividing this number by the number of days and the number of mice per cage. This method requires the assumption that each mouse drinks an equivalent amount of water.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
	Metric 18:	Sampling Adequacy	Medium	The study used cage vs. individual for body weight measurements, which is not the preferred experimental unit.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
	Metric 20:	Negative Control Response	High	Untreated mice were reported to show an expected result
Domain 6: Confoundir	ng / Variable Con	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Drinking water intake was graphically reported for the experimental, and control groups (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text discusses significant differences in drinking water intake results for other chemicals but does not report changes for this COI.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was clearly performed for some endpoints (text reports whether results were significant or not); however, the type of analysis (methods) used are not described.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 200427 Table: 3 of 4

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**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights; water intake

Effect(s):

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay **Duration:** 

Chemical: 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
1	Metric 24:	Reporting of Data	Low	Data were reported as means without measures of variance; control data were reported on separate graphs than the experimental data, making comparisons difficult. The dosing (as reported) is not particularly useful, and determining accurate dosing will be difficult using the data as presented. Statical analyses were not included in the graphs, although the text does not indicate any significant changes were observed.

Overall Quality Determination	High
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HERO ID: 200427 Table: 4 of 4

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

Effect(s):

Duration:

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 200427

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only
	Metric 5:	Positive Controls	N/A	A positive control is generally not required for this endpoint
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure Cl	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflon stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
		Administration		
	Metric 9:	Reporting of Doses/Concentrations	High	The doses were reported in mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group, the study Authors did report an Approximate weekly dose mg/kg body weight, however, the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously via drinking water for up to 52 weeks. This is acceptable for the endpoint(s) of interest
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Dose levels were based on preliminary studies and were justified by the study authors. Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three-dose levels for a carcinogenicity study, but appropriate for the endpoint of interest.
	Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.

Domain 4: Test Animals

HERO ID: 200427 Table: 4 of 4

### ... continued from previous page

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

Survival

Effect(s): **Duration:** 

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Parent compound

HERO ID: 200427

HERO ID:	200427			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
	Metric 15:	Number of Animals per Group	Low	The number of animals/group (35 males only/group) was acceptable for this outcome, however, OECD recommendations for a chronic study indicate both sexes should be evaluated.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Body weights were only recorded monthly and on a per-cage basis. The study does not specify how many mice were per cage. This is not a standard practice for body weight measurements. Drinking water consumption was measured weekly. The mean water intake (in grams) of each mouse per day was calculated by subtracting the weight of water after 1 week from the weight of the water at time of filing and dividing this number by the number of days and the number of mice per cage. This method requires the assumption that each mouse drinks an equivalent amount of water.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
	Metric 18:	Sampling Adequacy	Medium	The study used cage vs. individual for body weight measurements, which is not the preferred experimental unit.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
	Metric 20:	Negative Control Response	High	No mortalities were observed in negative control groups
Domain 6: Confoundin	ng / Variable Coi	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Drinking water intake was graphically reported for the experimental, and control groups (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text discusses significant differences in drinking water intake results for other chemicals but does not report changes for this COI.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was clearly performed for some endpoints but there was no indication statistical analysis was used for mortality. However, the text suggests no deaths were observed for this COI
	Metric 24:	Reporting of Data	Low	Mortality data for this COI was not clearly reported. It was not included in a list of other chemicals showing mortality, but the text did not explicitly report that no mortality was observed in these treated animals.

HERO ID: 200427 Table: 4 of 4

1,1-Dichloroethane

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**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Mortality

**Outcome(s):** 

**Reported Health** Survival

Effect(s):

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 200427

Domain Metric Rating Comments

**Overall Quality Determination** High

Study	Citation:
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Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weights; body length

Effect(s):

**Duration:** Chronic (>91 days) 6 months; dogs **Chemical:** 1,1-Dichloroethane- Parent compound

HERO ID:	19/3131			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively using standard nomenclature; CASRN was not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
-	Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Ch	aracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group (per chemical). Two chamber sizes were used; it is unclear which chamber size the air-only controls were in. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months on alternate days (75 days total); this frequency is less than guideline recommendations.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for a chronic repeat exposure, this is less than guide- line recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Low	A whole-body dynamic air chamber was used for an inhalation study, the airflow rate (only reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animals	s			
	Metric 13:	Test Animal Characteristics	Low	Species, sex, and age were reported. Mongrel dogs were used, which makes comparisons between the control and exposure groups difficult. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Insufficient information on animal husbandry conditions was reported (only the type of food was provided)

HERO ID: 1973131 Table: 1 of 7

### ... continued from previous page

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights; body length

Effect(s):

**Duration:** Chronic (>91 days) 6 months; dogs **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	Only a single male dog/group was used; the low number decreases the ability to characterize or observe a toxic effect.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	It was reported that weights were followed weekly.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of outcome assessment were not clearly reported. However, control and exposed dogs were evaluated after the same duration of exposure.
	Metric 18:	Sampling Adequacy	Low	Single animals were used for all endpoints.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Medium	The study authors did not indicate whether or not the control dog responses were unexpected.
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures.  Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis could not be performed due to an n of 1
	Metric 24:	Reporting of Data	High	Growth results were displayed graphically and were appropriate given the limitations in sample size. Body weights and pathology results were adequately reported.

# **Overall Quality Determination**

## Medium

HERO ID: 1973131 Table: 2 of 7

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

Survival

**Effect(s):** 

**Duration:** Chronic (>91 days) 6 months; dogs **Chemical:** 1,1-Dichloroethane- Parent compound

HERO ID:	19/3131			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively using standard nomenclature; CASRN was not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Ch	naracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group (per chemical). Two chamber sizes were used; it is unclear which chamber size the air-only controls were in. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months on alternate days (75 days total); this frequency is less than guideline recommendations.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for a chronic repeat exposure, this is less than guide- line recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Low	A whole-body dynamic air chamber was used for an inhalation study, the airflow rate (only reported to be "comfortable") and the rate of air change were not reported.
D : 4 T : 4 : 1				
Domain 4: Test Animals		Trat Assissal Characteristics	T	0 ' 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	Metric 13:	Test Animal Characteristics	Low	Species, sex, and age were reported. Mongrel dogs were used, which makes comparisons between the control and exposure groups difficult. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Insufficient information on animal husbandry conditions were reported (type of food was reported)
	Metric 15:	Number of Animals per Group	Low	Only a single male dog/group was used; this is considered to be low, but may be considered acceptable for dogs

HERO ID: 1973131 Table: 2 of 7

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		contin	ued from p	revious page		
Study Citation: Health Outcome(s):	Mellon Insti Mortality	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.  Mortality				
Reported Health	Survival					
Effect(s):	Survivar					
Duration:	Chronic (>9	1 days) 6 months; dogs				
Chemical:		bethane- Parent compound				
HERO ID:	1973131	•				
Domain		Metric	Rating	Comments		
Domain 5: Outcome A	Assessment					
	Metric 16:	Outcome Assessment Methodology	Low	Beyond a list of what outcomes were evaluated, minimal details of the methods of outcome assessment were described. The frequency of animal observation was not reported.		
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of outcome assessment were not clearly reported. However, control and exposed dogs were evaluated after the same duration of exposure.		
	Metric 18:	Sampling Adequacy	Low	All animals were observed for mortality.		
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated		
	Metric 20:	Negative Control Response	High	Results for the control dog were as expected (no death)		
Domain 6: Confoundi	ng / Variable Co	ntrol				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.		
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis could not be performed due to an n of 1		
	Metric 24:	Reporting of Data	Low	Results were reported in the text as a negative outcome (no mortalities)		
Overall Qual	lity Detern	nination	Low			

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

**Study Citation:** 

Health Outcome(s): Reported Health Effect(s):	Hepatic/Live mune/Hema Hepatic/Live	tological; Endocrine (Endocrine (thyroid, par er: Live weights, histopathology; Reproducti	(thyroid, parath athyroid, Panci ve/Developme	yroid, Pancreas, Adrenal); Renal/Kidney; Cardiovascular; Lung/Respiratory; Im-
Duration: Chemical: HERO ID:	Blood cell of histopatholo Chronic (>9	counts and hemoglobin determinations; Sple		ogy; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Adrenal
Domain		Metric	Rating	Comments
Domain 1: Test Substance	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively using standard nomenclature; CASRN was not provided.
	Metric 2:	Test Substance Source	Low	All Outcomes: A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	All Outcomes: Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Ch	aracterization			
Domain 3. Exposure Cit	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: The study consisted of only a single exposure group (per chemical). Two chamber sizes were used; it is unclear which chamber size the air-only controls were in. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: Reported as 7hrs/day for 6 months on alternate days (75 days total); this frequency is less than guideline recommendations.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: A whole-body dynamic air chamber was used for an inhalation study, the airflow rate (only reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animals	<b>.</b>			
	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Species, sex, and age were reported. Mongrel dogs were used, which makes comparisons between the control and exposure groups difficult. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure
		Continu	ued on next pa	age

Study Citation:

Health
Outcome(s):
Reported Health
Effect(s):
Blood cell counts and hemoglobin determinations; Spleen histopathology;
Duration:

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Hepatic/Liver; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Testis histopathology; Renal/Kidney: Kidney weights and histopathology; serum BUN; Cardiovascular: Histology; Lung/Respiratory: Histopathology; Immune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Adrenal histopathology;
Chronic (>91 days) 6 months; dogs

Duration: Chronic (>91 days) 6 months; dogs
Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 1973131

Domain	Metric	Rating	Comments
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Insufficient information on animal husbandry conditions was reported (only the type of food was provided)
Metric 15:	Number of Animals per Group	Low	All Outcomes: Only a single male dog/group was used; the low number decreases the ability to characterize or observe a toxic effect.

#### Domain 5: Outcome Assessment

Metric 16: Outcome Assessment Methodology Medium

Hepatic/Liver: The outcome assessment methodology was appropriate, (e.g., organ weights, histopathology, serum chemistry/hematology), however, some details were limited (e.g., for histology, no information regarding the number of slides or staining used). Methods for the thymol-barbital test was cited to another publication. Limited to no details of methods of the brom sulfalein retention test were provided.; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Only histology for this endpoint was performed; information regarding the number of slides or staining used.; Renal/Kidney: The outcome assessment methodology was appropriate, (e.g., organ weights, histopathology, serum chemistry/hematology), however, some details were limited (e.g., for histology, no information regarding the number of slides or staining used).; Cardiovascular: The outcome assessment methodology was appropriate, (e.g., organ weights, histopathology, serum chemistry/hematology), however, some details were limited (e.g., for histology, no information regarding the number of slides or staining used).; Lung/Respiratory: Only histology for this endpoint was performed; information regarding the number of slides or staining used.; Immune/Hematological: The outcome assessment methodology was appropriate, (e.g., organ weights, histopathology, serum chemistry/hematology), however, some details were limited (e.g., for histology, no information regarding the number of slides or staining used).; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Only histology for this endpoint was performed; information regarding the number of slides or staining used.

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Study Citation: Health Outcome(s): Reported Health Effect(s):	Hepatic/Live mune/Hema Hepatic/Live Renal/Kidne	tological; Endocrine (Endocrine (thyroid, par er: Live weights, histopathology; Reproducti ey: Kidney weights and histopathology; serur counts and hemoglobin determinations; Spla	(thyroid, parath rathyroid, Panci ive/Development n BUN; Cardio	yroid, Pancreas, Adrenal); Renal/Kidney; Cardiovascular; Lung/Respiratory; Im-
Duration: Chemical: HERO ID:	Chronic (>9	gy; 01 days) 6 months; dogs 0ethane- Parent compound		
Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment  Sampling Adequacy	Medium	Hepatic/Liver: Details of outcome assessment were not clearly reported for some outcomes (e.g., bromsulfalein, although dates of the collections between exposed and control dogs were equivalent, and thymol-barbital test). For other relevant outcomes, data for control and exposed dogs were consistently collected.; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Renal/Kidney: Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Cardiovascular: Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Lung/Respiratory: Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Immune/Hematological: Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Medium	All Outcomes: The study authors did not indicate whether or not the control dog responses were unexpected.
Domain 6: Confoundir	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.

HERO ID: 1973131 Table: 3 of 7

#### ... continued from previous page

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons. **Study Citation:** Health Hepatic/Liver; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Outcome(s): Hepatic/Liver: Live weights, histopathology; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Testis histopathology; Reported Health Renal/Kidney: Kidney weights and histopathology; serum BUN; Cardiovascular: Histology; Lung/Respiratory: Histopathology; Immune/Hematological: Effect(s): Blood cell counts and hemoglobin determinations; Spleen histopathology; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Adrenal histopathology; **Duration:** Chronic (>91 days) 6 months; dogs Chemical: 1,1-Dichloroethane- Parent compound HERO ID: 1973131 Rating Comments Domain Metric Metric 23: Data Presentation and Analysis N/A Hepatic/Liver: Statistical analysis was not possible for most endpoints (n=1), however, the study Authors applied statistical analysis in some cases (e.g., means of urea nitrogen and phosphate units derived from multiple collection times were compared to controls by the "t" test). Although this allows for some comparison even with use of single animals, it could dilute or mask changes occurring after longer exposure times and therefore may not be appropriate.; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Statistical analysis was not possible for most endpoints (n=1); Renal/Kidney: Statistical analysis was not possible for most endpoints (n=1); Cardiovascular: Statistical analysis was not possible for most endpoints (n=1); Lung/Respiratory: Statistical analysis was not possible for most endpoints (n=1); Immune/Hematological: Statistical analysis was not possible for most endpoints (n=1); Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Statistical analysis was not possible for most endpoints (n=1) Metric 24: Reporting of Data High All Outcomes: Individual animal data were provided for all endpoints.

### **Overall Quality Determination**

### Medium

HERO ID: 1973131 Table: 4 of 7

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weights; body length

Effect(s):

**Duration:** Chronic (>91 days) 6 months; rats 1,1-Dichloroethane- Parent compound Chemical:

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Identified as ethylidene chloride (1,1-dichloroethane); CASRN not provided
	Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Cl	haracterization			
, r	Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group. Two chamber sizes were used, and it is unclear if the air-only controls were in the same chamber size. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months; the frequency of exposure was not clearly stated. The text indicated that 75 exposure days had been completed. 75, 7-hr exposures over a span of 6 months (24 weeks) would be ~2 exposure days/week?
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for chronic repeat exposure, this is less than guidelin recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Medium	A whole body dynamic air chamber was used for an inhalation study, the air flow rate (reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animal	ls			
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and age were reported. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Information included # animals/cage (n=6), food and water. No other animal husbandry details were provided. It is unclear if housing conditions were appropriate given problems with animal infections,
	Metric 15:	Number of Animals per Group	Low	The number of animals (12/sex) is lower than guideline recommendations for a chronic study in rats

HERO ID: 1973131 Table: 4 of 7

1,1-Dichloroethane

### ... continued from previous page

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights; body length

Effect(s):

**Duration:** Chronic (>91 days) 6 months; rats **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Body weights were followed weekly
	Metric 17:	Consistency of Outcome Assessment	Low	Details of outcome assessment were not clearly reported (i.e, it is unclear what animals were included in the dataset, and whether the animals added after 30 days were pooled with the original group of animals that survived, as was indicated for some other endpoints).
	Metric 18:	Sampling Adequacy	Low	The number of animals contributing to the measurements are not reported.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Medium	Growth curves were provided. There is no indication the growth of the negative control animals was atypical although, this was not explicitly discussed.
Domain 6: Confound	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	A significant number of animals died to due apparent lung infections unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed on some endpoints, but the methods were not described.
	Metric 24:	Reporting of Data	Medium	Summary tables did not include measures of variance and the summary table for pathology data was ambiguously reported. Samples were described as "sets of tissues examined" and "sets with major pathology" without distinguishing between males and females, or if data were from animals exposed for 45 days (e.g., animals added midstudy), or 75 days. However, individual animal data were adequately presented in tables at the end of the study.

# **Overall Quality Determination**

# Uninformative

HERO ID: 1973131 Table: 5 of 7

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

Effect(s):

**Duration:** Chronic (>91 days) 6 months; rats 1,1-Dichloroethane- Parent compound Chemical:

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Identified as ethylidene chloride (1,1-dichloroethane); CASRN not provided
	Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Cl	haracterization			
, r	Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group. Two chamber sizes were used, and it is unclear if the air-only controls were in the same chamber size. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months; the frequency of exposure was not clearly stated. The text indicated that 75 exposure days had been completed. 75, 7-hr exposures over a span of 6 months (24 weeks) would be ~2 exposure days/week?
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for chronic repeat exposure, this is less than guidelin recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Medium	A whole body dynamic air chamber was used for an inhalation study, the air flow rate (reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animal	ls			
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and age were reported. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Information included # animals/cage (n=6), food and water. No other animal husbandry details were provided. It is unclear if housing conditions were appropriate given problems with animal infections,
	Metric 15:	Number of Animals per Group	Low	The number of animals (12/sex) is lower than guideline recommendations for a chronic study in rats

HERO ID: 1973131 Table: 5 of 7

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

Effect(s):

**Duration:** Chronic (>91 days) 6 months; rats 1,1-Dichloroethane- Parent compound Chemical:

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
Domain 5: Outcom	ne Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	Beyond a list of what outcomes were evaluated, minimal details of the methods of outcome assessment were described. The frequency of animal observation was not reported.
	Metric 17:	Consistency of Outcome Assessment	Low	Details of outcome assessment were not clearly reported.
	Metric 18:	Sampling Adequacy	High	All animals were observed for mortality
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Uninformative	The mortality rate of the control group was reported to be 57% (due to the presence of lung infections)
Domain 6: Confou	nding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	A significant number of animals died in all groups to due apparent lung infections unrelated to exposure. This significantly impacted the usefulness of this study.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was likely not performed due to the significant deaths resulting from lung infections in all groups (including the controls)
	Metric 24:	Reporting of Data	Medium	No direct comparisons were made with controls, but mortality rates for both controls and the exposed group was reported.

# **Overall Quality Determination**

## Uninformative

HERO ID: 1973131 Table: 6 of 7

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
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Health

Renal/Kidney

**Outcome(s):** 

Reported Health

Kidney weights and histopathology; serum BUN

Effect(s):

**Duration:** Chronic (>91 days) 6 months; rats **Chemical:** 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substar	ice			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively using standard nomenclature; CASRN was not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure C	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group. Two chamber sizes were used, and it is unclear if the air-only controls were in the same chamber size. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months; the frequency of exposure was not clearly stated. The text indicated that 75 exposure days had been completed. 75, 7-hr exposures over a span of 6 months (24 weeks) would be ~2 exposure days/week?
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Medium	A whole body dynamic air chamber was used for an inhalation study, the air flow rate (reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and age were reported. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Information included # animals/cage (n=6), food and water. No other animal husbandry details were provided. It is unclear if housing conditions were appropriate given problems with animal infections.

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health

Kidney weights and histopathology; serum BUN

**Effect(s):** 

**Duration:** Chronic (>91 days) 6 months; rats **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 197313

HERO ID:	19/3131			
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	The number of animals (12/sex) is lower than guideline recommendations for a chronic study in rats
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Outcome assessment methods were appropriate, but were poorly described (e.g., no details on tissue collection, histology methods used, etc.,)
	Metric 17:	Consistency of Outcome Assessment	Low	Details of outcome assessment were not clearly reported (i.e, it is unclear what animals were included in the dataset, and whether the animals added after 30 days were pooled with the original group of animals that survived, as was indicated for some other endpoints).
	Metric 18:	Sampling Adequacy	Low	The number of animals contributing to the measurements are not reported.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Uninformative	57% of control animals died; Roughly 50% of control animals evaluated had major pathology of the kidney (25%), liver (30%), or lung (29%).
Domain 6: Confoun	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	Animals from all groups were reported to have a virus, or pleurpneumonia like organism/infection. This significantly affected the reliability of this study
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was not performed; it is presumed this is due to the poor health of the control animals. Statistical analysis was performed for organ weights; however, the methods were not adequately described.
	Metric 24:	Reporting of Data	Low	Summary tables did not include measures of variance and the summary table for pathology data was ambiguously reported. Samples were described as "sets of tissues examined" and "sets with major pathology" without distinguishing between males and females, or if data were from animals exposed for 45 days (e.g., animals added midstudy), or 75 days. However, individual animal data were adequately presented in tables at the end of the study.

# **Overall Quality Determination**

## Uninformative

**Study Citation:** Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Reproductive/Developmental; Hepatic/Liver; Endocrine; Immune/Hematological; Lung/Respiratory; Cardiovascular;

**Outcome(s):** 

Reported Health Effect(s):

Reproductive/Developmental: Testis histopathology; Hepatic/Liver: Live weights, histopathology; Endocrine: Adrenal histopathology; Immune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Lung/Respiratory: Histopathology; Cardiovascular:

Histology;

Duration: Chemical: Chronic (>91 days) 6 months; rats 1,1-Dichloroethane- Parent compound

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric	1: Test Substance Identity	High	Reproductive/Developmental: Identified as ethylidene chloride (1,1-dichloroethane); CASRN not provided; Hepatic/Liver: Identified as ethylidene chloride (1,1-dichloroethane); CASRN not provided; Endocrine: The test substance was identified definitively using standard nomenclature; CASRN was not provided.; Immune/Hematological: The test substance was identified definitively using standard nomenclature; CASRN was not provided.; Lung/Respiratory: Identified as propylene dichloride (1,2-dichloropropane); CASRN not provided; Cardiovascular: The test substance was identified definitively using standard nomenclature; CASRN was not provided.
Metric	2: Test Substance Source	Low	All Outcomes: A commercial source was identified; batch and lot numbers were not provided.
Metric	3: Test Substance Purity	Low	All Outcomes: Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design			
Metric	4: Negative and Vehicle Controls	High	All Outcomes: The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
Metric	5: Positive Controls	N/A	All Outcomes: Not necessary for the study type
Metric	6: Randomized Allocation of Animals	Low	All Outcomes: Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Characteriza	ation		
Metric	7: Preparation and Storage of Test Substance	Low	All Outcomes: The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
Metric	8: Consistency of Exposure Administration	Medium	All Outcomes: The study consisted of only a single exposure group. Two chamber sizes were used, and it is unclear if the air-only controls were in the same chamber size. However, the text indicates that all chambers had an equivalent rate of air change.
Metric	9: Reporting of Doses/Concentrations	High	All Outcomes: Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
Metric	10: Exposure Frequency and Duration	Low	All Outcomes: Reported as 7hrs/day for 6 months; the frequency of exposure was not clearly stated. The text indicated that 75 exposure days had been completed. 75, 7-hr exposures over a span of 6 months (24 weeks) would be ~2 exposure days/week?

HERO ID: 1973131 Table: 7 of 7

### ... continued from previous page

**Study Citation:** Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

**Health** Reproductive/Developmental; Hepatic/Liver; Endocrine; Immune/Hematological; Lung/Respiratory; Cardiovascular;

**Outcome(s):** 

**Reported Health** Reproductive/Developmental: Testis histopathology; Hepatic/Liver: Live weights, histopathology; Endocrine: Adrenal histopathology; Immune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Lung/Respiratory: Histopathology; Cardiovascular:

Histology;

**Duration:** Chronic (>91 days) 6 months; rats **Chemical:** 1,1-Dichloroethane- Parent compound

HERO ID:	1973131

Domain	Metric	Rating	Comments
Metric	1: Number of Exposure Groups and Dose/Concentration Spacing	Low	Reproductive/Developmental: A single exposure group was used for chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Hepatic/Liver: A single exposure group was used for chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Endocrine: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Immune/Hematological: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Lung/Respiratory: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Cardiovascular: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.
Metric 1	2: Exposure Route and Method	Medium	All Outcomes: A whole body dynamic air chamber was used for an inhalation study, the air flow rate (reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animals			
Metric	3: Test Animal Characteristics	Medium	All Outcomes: Species, strain, sex, and age were reported. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
Metric	4: Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Information included # animals/cage (n=6), food and water. No other animal husbandry details were provided. It is unclear if housing conditions were appropriate given problems with animal infections,
Metric	5: Number of Animals per Group	Low	All Outcomes: The number of animals (12/sex) is lower than guideline recommendations for a chronic study in rats
Domain 5: Outcome Assessment			
Metric	6: Outcome Assessment Methodology	Medium	All Outcomes: Outcome assessment methods were appropriate, but were poorly described (e.g., no details on tissue collection, histology methods used, etc.,)
Metric 3	7: Consistency of Outcome Assessment	Low	All Outcomes: Details of outcome assessment were not clearly reported (i.e, it is unclear what animals were included in the dataset, and whether the animals added after 30 days were pooled with the original group of animals that survived, as was indicated for some other endpoints).
Metric	8: Sampling Adequacy	Low	All Outcomes: The number of animals contributing to the measurements are not reported.
Metric 1	8	N/A	All Outcomes: Not necessary for the endpoint evaluated
Metric 2	0: Negative Control Response	Uninformative	All Outcomes: 57% of control animals died; Roughly 50% of control animals evaluated had major pathology of the kidney (25%), liver (30%), or lung (29%).

HERO ID: 1973131 Table: 7 of 7

1,1-Dichloroethane

### ... continued from previous page

**Study Citation:** Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health Reproductive/Developmental; Hepatic/Liver; Endocrine; Immune/Hematological; Lung/Respiratory; Cardiovascular;

**Outcome(s):** 

**Reported Health** 

Reproductive/Developmental: Testis histopathology; Hepatic/Liver: Live weights, histopathology; Endocrine: Adrenal histopathology; Im-Effect(s): mune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Lung/Respiratory: Histopathology; Cardiovascular:

Histology;

**Duration:** Chronic (>91 days) 6 months; rats 1,1-Dichloroethane- Parent compound **Chemical:** 

**HERO ID:** 1973131

Domain	Metric	Rating	Comments
Domain 6: Confounding / Varial	le Control		
Metric	21: Confounding Variables in Test Design and Procedures	Low	All Outcomes: The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored
Metric	22: Health Outcomes Unrelated to Exposure	Uninformative	All Outcomes: Animals from all groups were reported to have a virus, or pleurpneumonia like organism/infection. This significantly affected the reliability of this study
Metri	23: Data Presentation and Analysis	Low	All Outcomes: Statistical analysis was not performed; it is presumed this is due to the poor health of the control animals. Statistical analysis was performed for organ weights; however, the methods were not adequately described.
Metric	24: Reporting of Data	Medium	All Outcomes: Summary tables did not include measures of variance and the summary table for pathology data was ambiguously reported. Samples were described as "sets of tissues examined" and "sets with major pathology" without distinguishing between males and females, or if data were from animals exposed for 45 days (e.g., animals added mid-study), or 75 days. However, individual animal data were adequately presented in tables at the end of the study.

# **Overall Quality Determination**

## Uninformative

HERO ID:

646679

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-
	107
Health	Renal/Kidney; Lung/Respiratory; endocrine (endocrine); Skin/Connective Tissue; Cancer/Carcinogenesis; Gastrointestinal; Reproductive/Developmental;
Outcome(s):	Cardiovascular;
Reported Health	Renal/Kidney: kidney and urinary bladder histopathology and gross pathology; Lung/Respiratory: Lung, bronchi, trachea histopathology and gross pathol-
Effect(s):	ogy; endocrine (endocrine): Pituitary, pancreas and adrenal gland histopathology and gross pathology; Skin/Connective Tissue: Skin histopathology and
	gross pathology; Cancer/Carcinogenesis: All tissues were examined for neoplasms; Gastrointestinal: Salivary gland, gall bladder, bile duct (mice only),
	esophagus, stomach, small and large intestine histopathology and gross pathology; Reproductive/Developmental: Testes, prostate, mammary gland, ovary,
	uterus histopathology and gross pathology; Cardiovascular: Heart histopathology and gross pathology;
<b>Duration:</b>	Chronic (>91 days) 78 weeks- mouse
Chemical:	1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substan	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	All Outcomes: Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated >99% purity.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The untreated control and treated animals were the same age (i.e., 5 weeks old) at the start of the experiment, while the vehicle controls were approximately 2 weeks older than mice in the other groups and therefore intubation started 2 weeks sooner.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Nominal doses were clearly reported in units of mg/kg. TWA doses were
				reported. Low and high doses were increased several times throughout the course of the study to account for observed lack of toxicity. Timing of dose adjustments are clearly reported in the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	High	study to account for observed lack of toxicity. Timing of dose adjustments are clearly
	Metric 10: Metric 11:	Exposure Frequency and Duration Number of Exposure Groups and Dose/Concentration Spacing	High Medium	study to account for observed lack of toxicity. Timing of dose adjustments are clearly reported in the study report. Analytical/measured doses were not reported.

			ued from p	2 0		
Study Citation:		Bioassay of 1,1-dichloroethane for possible	le carcinoge	nicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1		
Health	107. Renal/Kidne	y; Lung/Respiratory; endocrine (endocrine)	; Skin/Conn	ective Tissue; Cancer/Carcinogenesis; Gastrointestinal; Reproductive/Developmental		
Outcome(s):	Cardiovascular;					
Reported Health Effect(s):	Renal/Kidney: kidney and urinary bladder histopathology and gross pathology; Lung/Respiratory: Lung, bronchi, trachea histopathology and gross pathology; endocrine (endocrine): Pituitary, pancreas and adrenal gland histopathology and gross pathology; Skin/Connective Tissue: Skin histopathology and gross pathology; Cancer/Carcinogenesis: All tissues were examined for neoplasms; Gastrointestinal: Salivary gland, gall bladder, bile duct (mice only) esophagus, stomach, small and large intestine histopathology and gross pathology; Reproductive/Developmental: Testes, prostate, mammary gland, ovary uterus histopathology and gross pathology; Cardiovascular: Heart histopathology and gross pathology;					
Duration:		1 days) 78 weeks- mouse				
Chemical:	1,1-Dichloro	bethane- Parent compound				
HERO ID:	646679					
Domain		Metric	Rating	Comments		
Domain 4: Test Anima	als					
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported and were adequate.		
	Metric 15:	Number of Animals per Group	Low	All Outcomes: 50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.		
Domain 5: Outcome A	Accecement					
Domain 3: Outcome A	Metric 16:	Outcome Assessment Methodology	High	Renal/Kidney: Methodology for the histologic examination was adequately described and addressed the intended outcome. Clinical chemistry was not reported.; Lung/Respiratory: Methodology for the histologic examination was adequately described and addressed the intended outcome.; endocrine (endocrine): Methodology for the histologic examination was adequately described and addressed the intended outcome.; Skin/Connective Tissue: Methodology for the histologic examination was adequately described and addressed the intended outcome.; Cancer/Carcinogenesis: Methodology for the histologic examination was adequately described and addressed the intended outcome.; Gastrointestinal: Methodology for the histologic examination was adequately described and addressed the intended outcome.; Reproductive/Developmental: Methodology for the histologic examination was adequately described and addressed the intended outcome.; Cardiovascular: Methodology for the histologic examination was adequately described and addressed the intended outcome.		
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.		
	Metric 18:	Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling (all animals were examined for histology).		
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for initial histology review.		
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control response was adequate.		
Domain 6: Confoundi	ng / Variable Co	ntral				
Domain 6: Confoundi	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: the study did not report all information to determine confounding but reported information did not identify differences		
		Conti	nued on nex	t nago		

<b>Study Citation:</b>		Bioassay of 1,1-dichloroethane for pos	ssible carcinoge	nicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-		
Health	107. Renal/Kidne	y; Lung/Respiratory; endocrine (endocr	rine); Skin/Conn	ective Tissue; Cancer/Carcinogenesis; Gastrointestinal; Reproductive/Developmental;		
Outcome(s):	Cardiovascular;					
Reported Health	Renal/Kidney: kidney and urinary bladder histopathology and gross pathology; Lung/Respiratory: Lung, bronchi, trachea histopathology and gross pathology					
Effect(s):	ogy; endocrine (endocrine): Pituitary, pancreas and adrenal gland histopathology and gross pathology; Skin/Connective Tissue: Skin histopathology and gross pathology; Cancer/Carcinogenesis: All tissues were examined for neoplasms; Gastrointestinal: Salivary gland, gall bladder, bile duct (mice only), esophagus, stomach, small and large intestine histopathology and gross pathology; Reproductive/Developmental: Testes, prostate, mammary gland, ovary,					
<b>Duration:</b>	uterus histopathology and gross pathology; Cardiovascular: Heart histopathology and gross pathology; Chronic (>91 days) 78 weeks- mouse					
Chemical:	1,1-Dichloro	bethane- Parent compound				
HERO ID:	646679	•				
Domain		Metric	Rating	Comments		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: Survival was low in the untreated male group compared to vehicle treated male group. This is unlikely to substantially impact results, as the vehicle treated controls can be used for dose-response analysis.		
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were clearly described and appropriate for the dataset.		
	Metric 24:	Reporting of Data	High	All Outcomes: Incidence data is adequately reported for all treatment groups by sex.		
Overall Qual	lity Detern	nination	High			

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Mortality Health

**Outcome(s):** 

**Reported Health** 

survival

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- mouse **Chemical:** 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated >99% purity.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The untreated control and treated animals were the same age (i.e., 5 weeks old) at the start of the experiment, while the vehicle controls were approximately 2 weeks older than mice in the other groups and therefore intubation started 2 weeks sooner.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	aracterization			
·	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were increased several times throughout the course of the study to account for observed lack of toxicity. Timing of dose adjustments are clearly reported in the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	High	Mice were treated with test substance 5 days/week for 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.
Domain 4: Test Animals	:			
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
		Contin	nued on nex	t page

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Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):							
Health	107.							
Outcome(s):	Mortality							
Reported Health	survival							
Effect(s):	Survivar							
Duration:	Chronic (>01 days) 78 weeks, mouse							
Chemical:	Chronic (>91 days) 78 weeks- mouse 1,1-Dichloroethane- Parent compound							
HERO ID:	646679							
	040079							
Domain		Metric	Rating	Comments				
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required				
				by OECD TG 451, which states at least 50 animals of each sex should be included in the				
				concurrent control groups.				
Domain 5: Outcome	Assessment							
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome (animals were inspected daily for mortality).				
	Metric 17:	Consistency of Outcome Assessment	High	All animals were inspected daily for mortality.				
	Metric 18:	Sampling Adequacy	High	Sampling was adequate. All animals in each group were inspected daily for mortality.				
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this outcome.				
	Metric 20:	Negative Control Response	Medium	Survival was adequate in vehicle (male and female) and untreated (female) control groups. However, Survival was low (35%) in the untreated males. However, because survival was adequate in the vehicle treated males, which is the most appropriate group to use for comparisons to the treated animals, this effect is unlikely to have substantial impact on results.				
Domain 6: Confound	ing / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design	Medium	the study did not report all information to determine confounding but reported informa-				
		and Procedures		tion did not identify differences				
	Metric 22:	Health Outcomes Unrelated to	Medium	Survival was low in the untreated male group compared to vehicle treated male group.				
		Exposure		This is unlikely to substantially impact results, as the vehicle treated controls can be used for dose-response analysis.				
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.				
	Metric 24:	Reporting of Data	High	Survival data were presented graphically for all control and treatment groups by sex.				
Overall Qua	lity Deterr	mination	High					

# **Overall Quality Determination**

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Hepatic/Liver Health

**Outcome(s):** 

**Reported Health** 

Liver histopathology and gross pathology

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- mouse 1,1-Dichloroethane- Parent compound **Chemical:** 

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated >99% purity.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The untreated control and treated animals were the same age (i.e., 5 weeks old) at the start of the experiment, while the vehicle controls were approximately 2 weeks older than mice in the other groups and therefore intubation started 2 weeks sooner.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	aracterization			
·	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were increased several times throughout the course of the study to account for observed lack of toxicity. Timing of dose adjustments are clearly reported in the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	High	Mice were treated with test substance 5 days/week for 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.
Domain 4: Test Animals	3			
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
		Conti	nued on nex	t nage

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Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-						
Health	107. Hepatic/Liver						
Outcome(s):	Tiepatie/Livei						
Reported Health	Liver history	athology and gross pathology					
Effect(s):	21. Cr mstop.	amerogy and gross pamerogy					
Duration:	Chronic (>9	1 days) 78 weeks- mouse					
Chemical:		bethane- Parent compound					
HERO ID:	646679	-					
Domain		Metric	Rating	Comments			
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.			
Domain 5: Outcome	Assessment						
	Metric 16:	Outcome Assessment Methodology	High	Methodology for the histologic examination was adequately described and addressed the intended outcome. Clinical chemistry and organ weight was not reported.			
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.			
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).			
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.			
	Metric 20:	Negative Control Response	High	Negative control response was adequate.			
Domain 6: Confound	ing / Variable Cor	ntrol					
	Metric 21:	Confounding Variables in Test Design	Medium	the study did not report all information to determine confounding but reported informa-			
		and Procedures		tion did not identify differences			
	Metric 22:	Health Outcomes Unrelated to	Medium	Survival was low in the untreated male group compared to vehicle treated male group.			
		Exposure		This is unlikely to substantially impact results, as the vehicle treated controls can be used for dose-response analysis.			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.			
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported for all treatment groups by sex.			

Study Citation: NCI (1978). Bioassay of 1.1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1
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107. Thyroid

Health

**Outcome(s):** 

**Reported Health** 

Thyroid histopathology and gross pathology

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- mouse Chemical: 1,1-Dichloroethane- Parent compound

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1		High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
Metric 2	: Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
Metric 3	: Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Design			
Metric 4	: Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The untreated control and treated animals were the same age (i.e., 5 weeks old) at the start of the experiment, while the vehicle controls were approximately 2 weeks older than mice in the other groups and therefore intubation started 2 weeks sooner.
Metric 5	: Positive Controls	N/A	Not necessary for this study type.
Metric 6	: Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterizat	ion		
Metric 7		High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
Metric 8	: Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
Metric 9	: Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were increased several times throughout the course of the study to account for observed lack of toxicity. Timing of dose adjustments are clearly reported in the study report. Analytical/measured doses were not reported.
Metric 1	0: Exposure Frequency and Duration	High	Mice were treated with test substance 5 days/week for 78 weeks.
Metric 1		Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
Metric 1	2: Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.
D1- 4. T+ A.:1-			
Domain 4: Test Animals  Metric 1	3: Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
Metric 1	4: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.

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Study Citation:	NCI (1978). 107.	Bioassay of 1,1-dichloroethane for possible	le carcinoge	nicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1				
Health	Thyroid							
Outcome(s):	·							
Reported Health	Thyroid hist	opathology and gross pathology						
Effect(s):								
Duration:	Chronic (>9	1 days) 78 weeks- mouse						
Chemical:		bethane- Parent compound						
HERO ID:	646679							
Domain		Metric	Rating	Comments				
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.				
Domain 5: Outcome A	ssessment							
	Metric 16:	Outcome Assessment Methodology	High	Methodology for the histologic examination was adequately described and addressed the intended outcome.				
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.				
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).				
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.				
	Metric 20:	Negative Control Response	Medium	Negative control response was adequate.				
Domain 6: Confoundir	o / Variable Co	ntrol						
community of Companion	Metric 21:	Confounding Variables in Test Design	Medium	the study did not report all information to determine confounding but reported informa-				
		and Procedures		tion did not identify differences				
	Metric 22:	Health Outcomes Unrelated to	Medium	Survival was low in the untreated male group compared to vehicle treated male group.				
		Exposure		This is unlikely to substantially impact results, as the vehicle treated controls can be used for dose-response analysis.				
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.				
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported for all treatment groups by sex.				

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

Health Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weight (6 week and 78 week study), food consumption (78 week study only)

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- mouse **Chemical:** 1,1-Dichloroethane- Parent compound

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The untreated control and treated animals were the same age (i.e., 5 weeks old) at the start of the experiment, while the vehicle controls were approximately 2 weeks older than mice in the other groups and therefore intubation started 2 weeks sooner.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Char	racterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were increased several times throughout the course of the study to account for observed lack of toxicity. Timing of dose adjustments are clearly reported in the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	High	Mice were treated with test substance 5 days/week for 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.

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Study Citation:	NCI (1978).	Bioassay of 1,1-dichloroethane for possible	le carcinoge	nicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):			
Health	107.	Matahalia					
	Nutritional/Metabolic						
Outcome(s):	Dody waight	(6 week and 70 week study) food consum	ntion (70 mg	sale attuder andre)			
Reported Health Effect(s):	Body weight	(6 week and 78 week study), food consum	puon (76 we	eck study only)			
Duration:	Chronic (>0	1 days) 78 weeks- mouse					
Chemical:		ethane- Parent compound					
HERO ID:	646679	ediane- i arciit compound					
Domain		Metric	Rating	Comments			
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.			
Domain 5: Outcome As	sessment						
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest. Body weight and food consumption was measured at weekly intervals for the first 10 weeks, and then monthly thereafter.			
	Metric 17:	Consistency of Outcome Assessment	Medium	Body weight and food consumption was measured at weekly intervals for the first 10 weeks, and then monthly thereafter. Exact timing of the assessment was not reported, however, this is unlikely to substantially impact results.			
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling			
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome being measured.			
	Metric 20:	Negative Control Response	Medium	Control animals appeared to gain weight adequately throughout the study period.			
Domain 6: Confounding	/ Variable Cor	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Survival was low in the untreated male group compared to vehicle treated male group. This is unlikely to substantially impact results, as the vehicle treated controls can be used for dose-response analysis.			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.			
	Metric 24:	Reporting of Data	Medium	Growth curves are provided to show changes in body weight. Food consumption data is not reported.			

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for	possible carcinogenicity. National Cancer Institute	e Carcinogenesis Technical Report Series 66(1978):1-
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107. Immune/Hematological Health

**Outcome(s):** 

**Reported Health** 

Bone marrow, spleen, lymph nodes, thymus histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- mouse Chemical: 1,1-Dichloroethane- Parent compound

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1		High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
Metric 2	: Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
Metric 3	: Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Design			
Metric 4	: Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The untreated control and treated animals were the same age (i.e., 5 weeks old) at the start of the experiment, while the vehicle controls were approximately 2 weeks older than mice in the other groups and therefore intubation started 2 weeks sooner.
Metric 5	: Positive Controls	N/A	Not necessary for this study type.
Metric 6	: Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterizat	ion		
Metric 7		High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
Metric 8	: Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
Metric 9	: Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were increased several times throughout the course of the study to account for observed lack of toxicity. Timing of dose adjustments are clearly reported in the study report. Analytical/measured doses were not reported.
Metric 1	0: Exposure Frequency and Duration	High	Mice were treated with test substance 5 days/week for 78 weeks.
Metric 1		Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
Metric 1	2: Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.
D1- 4. T+ A.:1-			
Domain 4: Test Animals  Metric 1	3: Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
Metric 1	4: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.

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Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-						
Health	107. Immune/Hematological						
Outcome(s):	minune/Tematological						
Reported Health	Bone marrov	w, spleen, lymph nodes, thymus histopathological	ogy and gros	ss pathology			
Effect(s):							
Ouration:		1 days) 78 weeks- mouse					
Chemical:		ethane- Parent compound					
HERO ID:	646679						
Domain		Metric	Rating	Comments			
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.			
Domain 5: Outcome As	ssessment						
	Metric 16:	Outcome Assessment Methodology	Medium	Methodology for the histologic examination was adequately described and partially addressed the intended outcome. Hematology was not measured.			
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.			
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).			
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.			
	Metric 20:	Negative Control Response	High	Negative control response was adequate.			
Domain 6: Confoundin	g / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Survival was low in the untreated male group compared to vehicle treated male group. This is unlikely to substantially impact results, as the vehicle treated controls can be used for dose-response analysis.			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.			
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported for all treatment groups by sex.			

## **Overall Quality Determination**

High

HERO ID: 646679 Table: 7 of 17

NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-**Study Citation:** Health endocrine (endocrine) Outcome(s): Reported Health Pituitary, pancreas and adrenal gland histopathology and gross pathology Effect(s): **Duration:** Chronic (>91 days) 78 weeks- rat Chemical: 1,1-Dichloroethane- Parent compound **HERO ID:** 646679 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3). Test Substance Source Metric 2: High Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified. Metric 3: Test Substance Purity High The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated >99% purity. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun. Positive Controls N/A Metric 5: Not necessary for this study type. Metric 6: Randomized Allocation of Animals Medium The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test High Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "con-Substance sidered generally stable for 10 days under the indicated storage conditions." Metric 8: Consistency of Exposure Medium Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported. Administration Metric 9: Reporting of Doses/Concentrations Medium Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported. **Exposure Frequency and Duration** Low Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intu-Metric 10: bation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound. Metric 11: Number of Exposure Groups and Medium Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at Dose/Concentration Spacing least 3 dose groups should be included. Metric 12: Exposure Route and Method High The exposure route (oral) and method (gavage) were suited to the test substance. Domain 4: Test Animals

HERO ID: 646679 Table: 7 of 17

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**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

Health **Outcome(s):** 

endocrine (endocrine)

**Reported Health** 

Pituitary, pancreas and adrenal gland histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodology for the histologic examination was adequately described and addressed the intended outcome.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).
	Metric 19:	Blinding of Assessors	Low	Not necessary for initial histology review.
	Metric 20:	Negative Control Response	High	Negative control response was adequate.
Domain 6: Confoun	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported.

### **Overall Quality Determination**

HERO ID: 646679 Table: 8 of 17

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

**Health** Cardiovascular; Neurological/Behavioral; Hepatic/Liver;

**Outcome(s):** 

**Reported Health** Cardiovascular: Heart histopathology and gross pathology; Neurological/Behavioral: Brain histopathology and gross pathology; clinical observations;

**Effect(s):** Hepatic/Liver: Liver histopathology and gross pathology;

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	All Outcomes: Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated >99% purity.
Domain 2: Test Desig	2n			
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study did not report how animals were allocated to study groups.
D				
Domain 3: Exposure		D ( 15)	TT' 1	
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route (oral) and method (gavage) were suited to the test substance.

HERO ID: 646679 Table: 8 of 17

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**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

Health Cardiovascular; Neurological/Behavioral; Hepatic/Liver;

**Outcome(s):** 

Cardiovascular: Heart histopathology and gross pathology; Neurological/Behavioral: Brain histopathology and gross pathology; clinical observations; Reported Health

Effect(s): Hepatic/Liver: Liver histopathology and gross pathology;

**Duration:** Chronic (>91 days) 78 weeks- rat Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Low	All Outcomes: 50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Cardiovascular: Methodology for the histologic examination was adequately described.; Neurological/Behavioral: Outcome assessment (histology, clinical observations) was appropriate for the outcome of interest.; Hepatic/Liver: Methodology for the histologic examination was adequately described and addressed the intended outcome. Clinical chemistry and organ weight was not reported.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling (all animals were examined for histology).
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for initial histology review.
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control response was adequate.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	All Outcomes: The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Cardiovascular: Incidence data is adequately reported.; Neurological/Behavioral: Incidence data is adequately reported. Clinical observations were qualitatively described in text.; Hepatic/Liver: Incidence data is adequately reported.

HERO ID: 646679 Table: 8 of 17

1,1-Dichloroethane

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Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

**Health** Cardiovascular; Neurological/Behavioral; Hepatic/Liver;

**Outcome(s):** 

**Reported Health** Cardiovascular: Heart histopathology and gross pathology; Neurological/Behavioral: Brain histopathology and gross pathology; clinical observations;

**Effect(s):** Hepatic/Liver: Liver histopathology and gross pathology;

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain Metric Rating Comments

Overall Quality Determination Uninformative

HERO ID: 646679 Table: 9 of 17

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Skin/Connective Tissue Health

**Outcome(s):** 

**Reported Health** 

Skin histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat 1,1-Dichloroethane- Parent compound **Chemical:** 

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Design				
Ç	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.

Domain 4: Test Animals

HERO ID: 646679 Table: 9 of 17

#### ... continued from previous page

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

Skin/Connective Tissue Health

**Outcome(s):** 

**Reported Health** 

Skin histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodology for the histologic examination was adequately described and addressed the intended outcome.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.
	Metric 20:	Negative Control Response	Low	Negative control response was adequate.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported.

### **Overall Quality Determination**

HERO ID: 646679 Table: 10 of 17

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Mortality Health

**Outcome(s):** 

**Reported Health** 

survival

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Desig	ņ			
·	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure (	Characterization			
Donain 3. Exposure v	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.

Domain 4: Test Animals

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Mortality

Health

**Outcome(s):** 

Reported Health

survival

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome (animals were inspected daily for mortality).
	Metric 17:	Consistency of Outcome Assessment	High	All animals were inspected daily for mortality.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate. All animals in each group were inspected daily for mortality.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome being measured.
	Metric 20:	Negative Control Response	Uninformative	Survival was low in untreated (30% in males; 40% in females) and vehicle (5% in males; 20% in females) treated rats, which makes it difficult to detect an effect of treatment.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods (Kaplan-Meier analysis) were reported and were appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Survival data were presented graphically for all control and treatment groups by sex.

# **Overall Quality Determination**

HERO ID: 646679 Table: 11 of 17

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

Health Lung/Respiratory

**Outcome(s):** 

**Reported Health** 

Lung, bronchi, trachea histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Substan	nce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated >99% purity.
Domain 2: Test Design	l			
Č	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	haracterization			
Boniani 3. Exposure C	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.

Domain 4: Test Animals

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

**Health** Lung/Respiratory

**Outcome(s):** 

Reported Health

Lung, bronchi, trachea histopathology and gross pathology

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

HERO ID.	040077			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodology for the histologic examination was adequately described and addressed the intended outcome.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.
	Metric 20:	Negative Control Response	Uninformative	There was a high incidence of chronic murine pneumonia in untreated (70% in males; 85% in females) and vehicle control (95% in males; 89% in females) animals of both sexes. This was related to reduced survival of both sexes.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	Low	Incidence data is adequately reported.

### **Overall Quality Determination**

HERO ID: 646679 Table: 12 of 17

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

Health Reproductive/Developmental

**Outcome(s):** 

**Reported Health** 

Testes, prostate, mammary gland, ovary, uterus histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	araatarization			
Domain 5. Exposure Ci	Metric 7:	Preparation and Storage of Test	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and
	wiettie 7.	Substance	Ingn	stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.

Domain 4: Test Animals

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

Health

**Outcome(s):** 

**Reported Health** 

Testes, prostate, mammary gland, ovary, uterus histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat Chemical: 1,1-Dichloroethane- Parent compound

Reproductive/Developmental

**HERO ID:** 646679

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodology for the histologic examination was adequately described and addressed the intended outcome.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.
	Metric 20:	Negative Control Response	Low	Negative control response was adequate.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported.

### **Overall Quality Determination**

NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

HERO ID: 646679 Table: 13 of 17

1,1-Dichloroethane

**Study Citation:** 

Health Thyroid; Immune/Hematological; Outcome(s): Reported Health Thyroid: Thyroid histopathology and gross pathology; Immune/Hematological: Bone marrow, spleen, lymph nodes, thymus histopathology and gross Effect(s): pathology; **Duration:** Chronic (>91 days) 78 weeks- rat Chemical: 1,1-Dichloroethane- Parent compound **HERO ID:** 646679 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3). Metric 2: Test Substance Source High All Outcomes: Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified. All Outcomes: The test substance was reported as technical grade. Gas-liquid chro-Metric 3: Test Substance Purity High matography analysis indicated >99% purity. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun. Metric 5: Positive Controls N/A All Outcomes: Not necessary for this study type. Metric 6: Randomized Allocation of Animals Medium All Outcomes: The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test High All Outcomes: Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions Substance were "considered generally stable for 10 days under the indicated storage conditions." Metric 8: Consistency of Exposure Medium All Outcomes: Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported. Administration Metric 9: Reporting of Doses/Concentrations Medium All Outcomes: Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported. Metric 10: Exposure Frequency and Duration Low All Outcomes: Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound. Metric 11: Number of Exposure Groups and Medium All Outcomes: Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, Dose/Concentration Spacing which states at least 3 dose groups should be included. Metric 12: Exposure Route and Method High All Outcomes: The exposure route (oral) and method (gavage) were suited to the test substance. Continued on next page ...

		conti	inued from previou	s page	
Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-				
TT 1/1	107.	77			
Health	Thyroid; Im	mune/Hematological;			
Outcome(s):					
Reported Health	Thyroid: Th	yroid histopathology and gross pathology; Imi	mune/Hematological	: Bone marrow, spleen, lymph nodes, thymus histopathology and gross	
Effect(s):	pathology;				
Duration:	Chronic (>9	1 days) 78 weeks- rat			
Chemical:	1.1-Dichloro	pethane- Parent compound			
HERO ID:	646679	1			
Domain		Metric	Rating	Comments	
			-		
Domain 4: Test Animals	3				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported and were adequate.	
	Metric 15:	Number of Animals per Group	Low	All Outcomes: 50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex shoul be included in the concurrent control groups.	

Metric 16:	Outcome Assessment Methodology	Medium	Thyroid: Methodology for the histologic examination was adequately described and ad-
			dressed the intended outcome.; Immune/Hematological: Methodology for the histologic
			examination was adequately described and partially addressed the intended outcome.
			Hamatalagy was not massured

High All Outcomes: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.

All Outcomes: Incidence data is adequately reported.

Metric 18: High Sampling Adequacy All Outcomes: Reported information indicates the study used adequate sampling (all animals were examined for histology).

Metric 19: Blinding of Assessors N/A All Outcomes: Not necessary for initial histology review. Metric 20: Negative Control Response High All Outcomes: Negative control response was adequate.

Domain 6: Confounding / Variable Control

Metric 17:

Metric 24:

Domain 5: Outcome Assessment

Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: the study did not report all information to determine confounding but
	and Dracedures		reported information did not identify differences

and Procedures

Health Outcomes Unrelated to Uninformative Metric 22: All Outcomes: The high mortality in both sexes of rats appeared to be related to a high Exposure incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated,

low, and high dose groups of both sexes. Metric 23: Data Presentation and Analysis High All Outcomes: Statistical methods were clearly described and appropriate for the dataset.

**Overall Quality Determination** Uninformative

Reporting of Data

Consistency of Outcome Assessment

High

HERO ID: 646679 Table: 14 of 17

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

Health Gastrointestinal

**Outcome(s):** 

Reported Health

Salivary gland, gall bladder, bile duct (mice only), esophagus, stomach, small and large intestine histopathology and gross pathology

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>99\%$ purity.
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.

Domain 4: Test Animals

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

Health

Outcome(s):

Reported Health

Salivary gland, gall bladder, bile duct (mice only), esophagus, stomach, small and large intestine histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

Gastrointestinal

**HERO ID:** 646679

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Medium	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodology for the histologic examination was adequately described and addressed the intended outcome.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.
	Metric 20:	Negative Control Response	High	Negative control response was adequate.
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported.

### **Overall Quality Determination**

HERO ID: 646679 Table: 15 of 17

1,1-Dichloroethane

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Renal/Kidney Health

**Outcome(s):** 

**Reported Health** 

kidney and urinary bladder histopathology and gross pathology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Design	ı			
	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	horooterization			
Boniani 3. Exposure C	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.

Domain 4: Test Animals

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

Health Renal/Kidney

**Outcome(s):** 

Reported Health

kidney and urinary bladder histopathology and gross pathology

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Medium	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	Methodology for the histologic examination was adequately described and addressed the intended outcome. Clinical chemistry was not reported.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.
	Metric 20:	Negative Control Response	High	Negative control response was adequate.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported.

### **Overall Quality Determination**

HERO ID: 646679 Table: 16 of 17

**Study Citation:** NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107. Cancer/Carcinogenesis Health

**Outcome(s):** 

**Reported Health** 

All tissues were examined for neoplasms

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	High	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated >99% purity.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	paracterization			
Boiliain 3. Exposure Of	Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.

Domain 4: Test Animals

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-
Health	107. Cancer/Carcinogenesis

**Outcome(s):** 

Reported Health

All tissues were examined for neoplasms

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rat 1,1-Dichloroethane- Parent compound **Chemical:** 

**HERO ID:** 646679

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Low	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodology for the histologic examination was adequately described and addressed the intended outcome.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling (all animals were examined for histology).
	Metric 19:	Blinding of Assessors	N/A	Not necessary for initial histology review.
	Metric 20:	Negative Control Response	High	Negative control response was adequate.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Incidence data is adequately reported.

# **Overall Quality Determination**

HERO ID: 646679 Table: 17 of 17

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

Health Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weight (6 week and 78 week study), food consumption (78 week study only)

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
Domain 1: Test Substa				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,1-dichloroethane (Cas No. 75-34-3).
	Metric 2:	Test Substance Source	High	Test substance was obtained from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin) and the test substance identity was analytically verified.
	Metric 3:	Test Substance Purity	Medium	The test substance was reported as technical grade. Gas-liquid chromatography analysis indicated $>$ 99% purity.
Domain 2: Test Design	ı			
	Metric 4:	Negative and Vehicle Controls	High	Vehicle (received corn oil in volumes equal to those administered to high dose group) and untreated control groups were included. The vehicle and treated animals were the same age (i.e., 8 weeks old) at the start of the experiment, while the untreated controls were approximately 6 weeks younger than the other rat groups were included in the study ~4 weeks after intubation of the other groups had begun.
	Metric 5:	Positive Controls	N/A	Not necessary for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	haracterization			
Boniani 3. Exposure C	Metric 7:	Preparation and Storage of Test Substance	High	Test substance was prepared in corn oil. Fresh solutions were prepared weekly and stored at 1 degree Celsius. Study authors report that the prepared solutions were "considered generally stable for 10 days under the indicated storage conditions."
	Metric 8:	Consistency of Exposure Administration	Medium	Animals were administered test substance 5 days per week for 78 weeks. Gavage volume and daily timing of test substance administration were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Nominal doses were clearly reported in units of mg/kg. TWA doses were reported. Low and high doses were adjusted several times throughout the course of the study to account for observed lack of toxicity (i.e., in this case doses were increased) or excessive toxicity (in this case doses were decreased). Timing of dose adjustments are clearly reported in Table 1 of the study report. Analytical/measured doses were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Rats were gavaged 5d/week for the first 31 weeks of the experiment. On week 32, intubation was ceased for 1 week, followed by 4 weeks of intubation. This pattern (4 weeks of dosing, followed by 1 week of no dosing) was repeated until week 78. This dosage decrease was in response to the observed toxicity of the compound.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Initial doses were selected based on a preliminary range-finding study. Two treatment groups were included. This is few than recommended in OECD TG 451, which states at least 3 dose groups should be included.
	Metric 12:	Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance.

Domain 4: Test Animals

Study Citation: NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-

107.

Health Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weight (6 week and 78 week study), food consumption (78 week study only)

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- rat **Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 646679

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animals was obtained from a commercial source. Starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Medium	50 animals of each sex were included in the treatment groups, however, only 20 animals of each sex were included in the control groups. This is significantly less than required by OECD TG 451, which states at least 50 animals of each sex should be included in the concurrent control groups.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest. Body weight and food consumption was measured at weekly intervals for the first 10 weeks, and then monthly thereafter.
	Metric 17:	Consistency of Outcome Assessment	Medium	Body weight and food consumption was measured at weekly intervals for the first 10 weeks, and then monthly thereafter. Exact timing of the assessment was not reported, however, this is unlikely to substantially impact results.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome being measured.
	Metric 20:	Negative Control Response	High	Control animals appeared to gain weight adequately throughout the study period.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	the study did not report all information to determine confounding but reported information did not identify differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	The high mortality in both sexes of rats appeared to be related to a high incidence of pneumonia. Lesions of pneumonia were observed during the histologic examination of ~80% of rats and incidence of pneumonia was similar in vehicle, untreated, low, and high dose groups of both sexes.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for the dataset.
	Metric 24:	Reporting of Data	Medium	Growth curves are provided to show changes in body weight. Food consumption data is not reported.

### **Overall Quality Determination**

HERO ID: 62395 Table: 1 of 3

**Study Citation:** Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

Reproductive/Developmental

**Outcome(s): Reported Health** 

Litter effects, embryotoxicity, fetotoxicity

Effect(s):

**Duration:** Reproductive/Developmental Gestation days 6-15

1,1-Dichloroethane- Parent compound **Chemical:** 

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric Metric		High High	The test substance was specified clearly by chemical name (1,1-dichloroethane).  The source of the test substance was reported and included a lot number.
Metric	3: Test Substance Purity	High	Reagent-grade 1,1-dichloroethane was used. However, an analysis of the test material was performed, indicating that the volume of 1,1-dichloroethane by weight in the sample was 99.7% (other minor sample components were shown in Table 2).
Domain 2: Test Design			
Metric	4: Negative and Vehicle Controls	High	The study reports that animals were exposed to 1,1-dichloroethane at two different concentrations, one in an initial experiment and another in a subsequent experiment. For each experiment, control animals were exposed concurrently to filtered air.
Metric	e 5: Positive Controls	N/A	Positive controls were not required by study type.
Metric	e 6: Randomized Allocation of Animals	Low	The manner by which animals were allocated to study groups was not reported.
Domain 2: Evnagura Characteris	ration		
Domain 3: Exposure Characteriz  Metric		Medium	The vapor generation process was briefly outlined ("generated by metering liquid at known rates into a temperature-controlled evaporating flask"). Storage conditions of the (volatile) test substance were not reported. Owing to methods used to ensure that proper exposure concentrations were maintained throughout the study, missing details are unlikely to have a substantial impact on the study results.
Metric	8: Consistency of Exposure Administration	High	Details of exposure administration suggest that animals were exposed consistently across study groups (7 hours/day on GDs 6-15 in dynamic chambers). The time of day exposures were administered was not reported; language in the report suggests exposures were simultaneous.
Metric	9: Reporting of Doses/Concentrations	High	Analytical, nominal, and target concentrations were reported. Analytical concentrations were measured 3 times during each daily exposure (for 10 days) by spectrophotometry; the mean of these measurements resulted in analytical concentrations within 10% of the nominal concentrations. Combustion conductivity analyses was also used to continuously monitor concentrations.
Metric	: 10: Exposure Frequency and Duration	High	The exposure frequency and duration were reported (i.e., 7 hours/day on GDs 6-15) and appropriate for evaluating the outcome of interest (i.e., developmental effects). Experiments of this type typically expose rats on GDs 6-15. Daily exposures slightly longer than the standard from applicable guidelines (6 hours/day) was not considered a study limitation.

Study Citation: Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

Reproductive/Developmental

Outcome(s):

Reported Health

Litter effects, embryotoxicity, fetotoxicity

Effect(s):

**Duration:** Reproductive/Developmental Gestation days 6-15

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 62395

Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	There were deficiencies in the number of dose groups utilized; two experiments were conducted, each using one 1,1-dichloroethane exposure group. No rationale for the exposure concentrations were provided other than "subanesthetic concentrations" were used. Studies of this type typically use three concentration levels plus a control group.
	Metric 12:	Exposure Route and Method	Medium	A dynamic whole-body chamber was used for vapors; the number of changes per hour was not reported.
Domain 4: Test Animals	<b>S</b>			
	Metric 13:	Test Animal Characteristics	Low	The source of the test animals was not reported. The species and strain, life-stage, and approximate starting body weights of the test animals were indicated.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not explicitly specified; the study report indicates that between exposures, animals were housed in cages, provided food and water ad libitum, and that the room was controlled for other factors (temperature, humidity, and light/dark cycle, not further specified).
	Metric 15:	Number of Animals per Group	Medium	It appears that at least 20 animals/group were used (i.e., exposed to 1,1-dichloroethane); this number of animals/group is the number typically used for studies of this type.
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	High	Based on the reference cited by the study report (HEROID = 65020), the methodology used to assess developmental effects appeared appropriate. Maternal animals were sacrificed on GD 21 to evaluate developmental endpoints (litter parameters, fetal body measurements, and external, soft tissue, and skeletal anomalies).
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently in all study groups (i.e., developmental endpoints were assessed after sacrifice on GD 21).
	Metric 18:	Sampling Adequacy	High	The litter was considered the experimental unit of observation for developmental toxicity endpoints.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not required by study type (not indicated in guidelines for this study type).
	Metric 20:	Negative Control Response	Low	The biological response of the individual negative control groups were not reported (with the exception of sternebral anomalies). Control data for each experiment were provided for sternebral anomalies; however, a high incidence of this effect was observed in one of the two control groups (61% of litters were affected compared up about 22% typically affected based on historical control data from NTP).

Domain 6: Confounding / Variable Control

Study Citation: Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health Reproductive/Developmental

**Outcome(s):** 

**Reported Health** Litter effects, embryotoxicity, fetotoxicity

**Effect(s):** 

**Duration:** Reproductive/Developmental Gestation days 6-15

**Chemical:** 1,1-Dichloroethane- Parent compound

**HERO ID:** 62395

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although not all data were reported on confounding, the available data did not identify differences among groups. Note: table legends reference starvation control groups (not mentioned in the methods section); it is unclear if this text was carryover from a similar study cited in the report (HEROID = 65020).
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Reported data do not indicate that health outcomes unrelated to exposure influenced the study results. Although data were not shown, the text states that maternal animals did not exhibit signs of toxicity.
	Metric 23:	Data Presentation and Analysis	High	Statistical analyses were briefly described in the cited reference (HEROID 65020). Fisher's exact test was used to evaluate the frequency of anomalies and resorptions; maternal and fetal measurements, liver weights, and ALT were analyzed by an analysis of variance and Dunnett's test or Tukey's test.
	Metric 24:	Reporting of Data	Low	The study does not differentiate among findings between the two control groups. Data for control groups were pooled for all endpoints except sternebral anomalies (because of a difference in the incidence of this effect among control groups). Data were reported for outcomes described in the methods.

### **Overall Quality Determination**

### Medium

Human Health Hazard Animal Toxicology Evaluation HERO ID: 62395 Table: 2 of 3

**Study Citation:** Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights and food consumption

Effect(s): **Duration:** 

Reproductive/Developmental Gestation days 6-15

Chemical: 1,1-Dichloroethane- Parent compound

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Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was specified clearly by chemical name (1,1-dichloroethane).
	Metric 2:	Test Substance Source	High	The source of the test substance was reported and included a lot number.
	Metric 3:	Test Substance Purity	High	Reagent-grade 1,1-dichloroethane was used. However, an analysis of the test material was performed, indicating that the volume of 1,1-dichloroethane by weight in the sample was 99.7% (other minor sample components were shown in Table 2).
Domain 2: Test Design				
J	Metric 4:	Negative and Vehicle Controls	High	The study reports that animals were exposed to 1,1-dichloroethane at two different concentrations, one in an initial experiment and another in a subsequent experiment. For each experiment, control animals were exposed concurrently to filtered air.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The manner by which animals were allocated to study groups was not reported.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	The vapor generation process was briefly outlined ("generated by metering liquid at known rates into a temperature-controlled evaporating flask"). Storage conditions of the (volatile) test substance were not reported. Owing to methods used to ensure that proper exposure concentrations were maintained throughout the study, missing details are unlikely to have a substantial impact on the study results.
	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration suggest that animals were exposed consistently across study groups (7 hours/day on GDs 6-15 in dynamic chambers). The time of day exposures were administered was not reported; language in the report suggests exposures were simultaneous.
	Metric 9:	Reporting of Doses/Concentrations	High	Analytical, nominal, and target concentrations were reported. Analytical concentrations were measured 3 times during each daily exposure (for 10 days) by spectrophotometry; the mean of these measurements resulted in analytical concentrations within 10% of the nominal concentrations. Combustion conductivity analyses was also used to continuously monitor concentrations.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were reported (i.e., 7 hours/day on GDs 6-15) and appropriate for evaluating the outcome of interest. Daily exposures slightly longer than the standard from applicable guidelines (6 hours/day) was not considered a study limitation.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	There were deficiencies in the number of dose groups utilized; two experiments were conducted, each using one 1,1-dichloroethane exposure group. No rationale for the exposure concentrations were provided other than "subanesthetic concentrations" were used. Studies of this type typically use three concentration levels plus a control group.

### Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

Study Citation: Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

Nutritional/Metabolic

Outcome(s): Reported Health

Body weights and food consumption

Effect(s): Duration:

Reproductive/Developmental Gestation days 6-15

Chemical:

1,1-Dichloroethane- Parent compound

Metric 12:	Metric	Rating	Comments
Metric 12:			
Wietrie 12.	Exposure Route and Method	Medium	A dynamic whole-body chamber was used for vapors; the number of changes per hour was not reported.
Metric 13:	Test Animal Characteristics	Low	The source of the test animals was not reported. The species and strain, life-stage, and approximate starting body weights of the test animals was indicated.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not explicitly specified; the study report indicates that between exposures, animals were housed in cages, provided food and water ad libitum, and that the room was controlled for other factors (temperature, humidity, and light/dark cycle, not further specified).
Metric 15:	Number of Animals per Group	Medium	It appears that at least 20 animals/group were used (i.e., exposed to 1,1-dichloroethane); this number of animals/group is the amount typically used for studies of this type.
essment			
Metric 16:	Outcome Assessment Methodology	High	The methodology used to assess body weights (measured on GDs 6, 13, and 21) and food consumption (measured in each animal every 2 days throughout exposure) appeared appropriate.
Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups (i.e., food consumption and body weights were assessed at the same time points).
Metric 18:	Sampling Adequacy	High	The study report indicated that all maternal animals were evaluated for food consumption and body weight endpoints.
Metric 19:	Blinding of Assessors	N/A	Blinding was not required by study type; outcomes were not subjective.
Metric 20:	Negative Control Response	Medium	The biological response of individual negative control groups were not reported; however, the biological responses of the negative control shown (based on pooled data) were adequate for food consumption and body weight endpoints.
/ Variable Cor	ntrol		
Metric 21:	Confounding Variables in Test Design	Medium	Although not all data were reported on confounding, the available data did not identify differences among groups.
Metric 22:	Health Outcomes Unrelated to Exposure	High	Reported data do not indicate that health outcomes unrelated to exposure influenced the study results. Although data were not shown, the text states that maternal animals did not exhibit signs of toxicity.
Metric 23:	Data Presentation and Analysis	High	Statistical analyses were briefly described in the cited reference (HEROID 65020).
	Metric 13: Metric 14:  Metric 15:  Metric 15:  Metric 16:  Metric 17:  Metric 18:  Metric 19:  Metric 20:  / Variable Cor  Metric 21:  Metric 22:	Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group  Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure	Metric 13: Test Animal Characteristics Low  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group Medium  Metric 16: Outcome Assessment Methodology High  Metric 17: Consistency of Outcome Assessment High  Metric 18: Sampling Adequacy High  Metric 19: Blinding of Assessors N/A  Metric 20: Negative Control Response Medium  / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure

HERO ID: 62395 Table: 2 of 3

#### ... continued from previous page

Study Citation: Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

Nutritional/Metabolic

Outcome(s):

**Reported Health** 

Body weights and food consumption

**Effect(s):** 

**Duration:** Reproductive/Developmental Gestation days 6-15

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 62395

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	Medium	Data presentation was adequate. Maternal food consumption (Table 5) and weight gain (Table 6) were slightly but statistically significantly decreased among rats exposed to 3000 or 6000 ppm 1,1-dichloroethane. At Gestation day 13, body weights were significantly different than controls for both doses. As noted previously, control data were pooled.

# Overall Quality Determination High

Study Citation: Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

Hepatic/Liver

**Outcome(s):** 

Reported Health

Liver weights, gross appearance/pathology and SGPT/ALT activity

**Effect(s):** 

**Duration:** Reproductive/Developmental Gestation days 6-15

Chemical: 1,1-Dichloroethane- Parent compound

**HERO ID:** 62395

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1	: Test Substance Identity	High	The test substance was specified clearly by chemical name (1,1-dichloroethane).
Metric 2	: Test Substance Source	High	The source of the test substance was reported and included a lot number.
Metric 3	: Test Substance Purity	High	Reagent-grade 1,1-dichloroethane was used. However, an analysis of the test material was performed, indicating that the volume of 1,1-dichloroethane by weight in the sample was 99.7% (other minor sample components were shown in Table 2).
Domain 2: Test Design			
Metric 4	: Negative and Vehicle Controls	High	The study reports that animals were exposed to 1,1-dichloroethane at two different concentrations, one in an initial experiment and another in a subsequent experiment. For each experiment, control animals were exposed concurrently to filtered air.
Metric 5	: Positive Controls	N/A	Positive controls were not required by study type.
Metric 6	: Randomized Allocation of Animals	Low	The manner by which animals were allocated to study groups was not reported.
Domain 3: Exposure Characteriza			
Metric 7	: Preparation and Storage of Test Substance	Medium	The vapor generation process was briefly outlined ("generated by metering liquid at known rates into a temperature-controlled evaporating flask"). Storage conditions of the (volatile) test substance were not reported. Owing to methods used to ensure that proper exposure concentrations were maintained throughout the study, missing details are unlikely to have a substantial impact on the study results.
Metric 8	: Consistency of Exposure Administration	High	Details of exposure administration suggest that animals were exposed consistently across study groups (7 hours/day on GDs 6-15 in dynamic chambers). The time of day exposures were administered was not reported; language in the report suggests exposures were simultaneous.
Metric 9	Reporting of Doses/Concentrations	High	Analytical, nominal, and target concentrations were reported. Analytical concentrations were measured 3 times during each daily exposure (for 10 days) by spectrophotometry; the mean of these measurements resulted in analytical concentrations within 10% of the nominal concentrations. Combustion conductivity analyses was also used to continuously monitor concentrations.
Metric 1	0: Exposure Frequency and Duration	High	The exposure frequency and duration were reported (i.e., 7 hours/day on GDs 6-15) and appropriate for evaluating the outcome of interest. Daily exposures slightly longer than the standard from applicable guidelines (6 hours/day) was not considered a study limitation.
Metric 1	1: Number of Exposure Groups and Dose/Concentration Spacing	Low	There were deficiencies in the number of dose groups utilized; two experiments were conducted, each using one 1,1-dichloroethane exposure group. No rationale for the exposure concentrations were provided other than "subanesthetic concentrations" were used.

## Human Health Hazard Animal Toxicology Evaluation

## ... continued from previous page

**Study Citation:** Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

**Outcome(s):** 

**Duration:** 

**Reported Health** Effect(s):

Liver weights, gross appearance/pathology and SGPT/ALT activity

Reproductive/Developmental Gestation days 6-15

**Chemical:** 1,1-Dichloroethane- Parent compound

Hepatic/Liver

HERO ID:	62395			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Medium	A dynamic whole-body chamber was used for vapors; the number of changes per hour was not reported.
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	Low	The source of the test animals was not reported. The species and strain, life-stage, and approximate starting body weights of the test animals was indicated.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not explicitly specified; the study report indicates that between exposures, animals were housed in cages, provided food and water ad libitum, and that the room was controlled for other factors (temperature, humidity, and light/dark cycle, not further specified).
	Metric 15:	Number of Animals per Group	Medium	It appears that at least 20 animals/group were used (i.e., exposed to 1,1-dichloroethane); this number of animals/group is the amount typically used for studies of this type.
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	Medium	The methods used evaluated liver toxicity by measuring SGPT/ALT activity, liver weights, and gross pathology. Liver histology was not performed, and SGPT/ALT data were collected for pregnant animals on GD 21 only (6 days after cessation of treatment)
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups (i.e., liver effects were assessed at the same time points).
	Metric 18:	Sampling Adequacy	High	Based on a study referenced in this report (HEROID 65020) and data provided in tables SGPT/ALT activity was evaluated in 10 pregnant animals/group; all livers were weighed and examined grossly.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not required by study type; outcomes were not subjective.
	Metric 20:	Negative Control Response	Medium	The biological response of the individual negative control groups were not reported; however, the biological responses of the negative control shown (based on pooled data) were adequate. There were presumably no effects on gross pathology in controls.
Domain 6: Confounding	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although not all data were reported on confounding, the available data did not identify differences among groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Reported data do not indicate that health outcomes unrelated to exposure influenced the study results. Although data were not shown, the text states that maternal animals did not exhibit signs of toxicity.
	Metric 23:	Data Presentation and Analysis	High	Statistical analyses were briefly described in the cited reference (HEROID 65020). Maternal endpoints (including liver effects) were analyzed by an analysis of variance and Dunnett's test or Tukey's test.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

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HERO ID: 62395 Table: 3 of 3

Study Citation: Schwetz, B.A., Leong, B.K., Gehring, P.J. (1974). Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in

rats. Toxicology and Applied Pharmacology 28(3):452-464.

Health

Outcome(s):

Reported Health

Liver weights, gross appearance/pathology and SGPT/ALT activity

Effect(s):

**Duration:** Reproductive/Developmental Gestation days 6-15

Chemical: 1,1-Dichloroethane- Parent compound

Hepatic/Liver

**HERO ID:** 62395

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Low	The study does not differentiate among findings between the two control groups (the
				amount of time between experiments was not specified). SGPT/ALT activity in pregnant
				rats exposed to 6000 ppm 1,1-dichloroethane was not determined.

# **Overall Quality Determination**

# Medium

Dow Chemica	al. (1947). Results of range-	finding toxicological studie	s on Ethylidene Dichloride.

Health

Irritation

**Outcome(s):** 

**Study Citation:** 

**Reported Health** 

.).

Skin irritation

**Effect(s):** 

**Duration:** Not reported "repeated application" **Chemical:** 1,1-Dichloroethane- Parent compound

HERO ID.	1773137			
Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			
	Metric 1:	Test Substance Identity	High	The cover page of the submission specifies 1,1-dichloroethane was used. The study report names the test material as "ethylidine dichloride." A structural and empirical formula was provided.
	Metric 2:	Test Substance Source	Low	The test substance was from the Dow Chemical stockroom; it was not specified whether it was analytically verified.
	Metric 3:	Test Substance Purity	Low	The purity and/or grade were not reported.
Domain 2: Test Desi	on			
Domain 2. Test Desi	Metric 4:	Negative and Vehicle Controls	N/A	Not necessary for the study type
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups
Domain 3: Exposure	Characterization			
r	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported. It is unclear whether a vehicle was used.
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported (e.g volume, or coverage area)
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	The exposure doses/concentrations or amounts of test substance were not reported resulting in serious flaws.
	Metric 10:	Exposure Frequency and Duration	Uninformative	Specific details on exposure frequency or duration were not reported.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The number of exposure groups or dosing were not reported
	Metric 12:	Exposure Route and Method	High	The route of exposure was appropriate for the study type
Domain 4: Test Anii	nals			
Domain 1. Test Time	Metric 13:	Test Animal Characteristics	Low	The strain, sex, age, starting body weights, and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Uninformative	The test suggests only a single rabbit was used which is considered unacceptable for a skin irritation study.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment methodology was not clearly reported
	Metric 17:	Consistency of Outcome Assessment	High	This question is not applicable if a single animal was used.
		Coi	ntinued on next page .	

**Study Citation:** 

Dow Chemical, (1947). Results of range-finding toxicological studies on Ethylidene Dichloride.

Health

Irritation

**Outcome(s):** 

Reported Health

Effect(s):
Duration:

**Chemical:** 

Skin irritation

Not reported "repeated application" 1,1-Dichloroethane- Parent compound

**HERO ID:** 1973137

Domain	Metric	Rating	Comments
Metric	8: Sampling Adequacy	Low	Details of sampling were not reported; this question may be not applicable if a single animal was used.
Metric	9: Blinding of Assessors	N/A	Blinding is not necessary for this study type.
Metric 2	0: Negative Control Response	N/A	Negative control use is not applicable for skin irritation studies.
Domain 6: Confounding / Variable Metric 2	21: Confounding Variables in Test Design and Procedures	Low Medium	No information to assess confounding was provided.  There was no information either to support or dismiss the suggestion that there were
Welle 2	Exposure	Wedium	differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 2	23: Data Presentation and Analysis	N/A	Statistical methods are not necessary for this study type.
Metric 2	4: Reporting of Data	Low	Signs of irritation were qualitatively reported in the text. No irritation scores were provided.

# **Overall Quality Determination**

# Uninformative

Human Health Hazard Animal Toxicology Evaluation

Study Citation: Natsyuk, M. V., Chekman, I. S. (1975). Content of nicotinamide coenzymes in liver and myocardium of rats poisoned with dichloroethane. Bulletin of

Experimental Biology and Medicine 79(4):408-409.

**Health** Mortality

**Outcome(s):** 

**Reported Health** Mortality

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single gavage **Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 5441424

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
Met	tric 1:	Test Substance Identity	Low	The reported test substance was dichloroethane. The CASRN and source of the test substance were not provided to confirm its identity. Ambiguity and the inability to confirm the isomer used is likely to have a substantial impact on the study results.
Met	tric 2:	Test Substance Source	Low	The test substance source was not reported.
Met	tric 3:	Test Substance Purity	Low	The test substance purity was not reported.
Domain 2: Test Design				
	tric 4:	Negative and Vehicle Controls	Low	Negative controls were included, but the it was unclear whether the negative control was untreated vs. a vehicle control), and the lack of details is likely to have a substantial impact on results.
Met	tric 5:	Positive Controls	N/A	Positive controls were not necessary for the study type.
Met	tric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 2. Eurosum Clarate				
Domain 3: Exposure Characte Met	tric 7:	Preparation and Storage of Test Substance	Medium	The test substance was administered as a 20% solution in sunflower oil. Details on preparation were not provided. Information on storage was not reported, although due to the acute nature of the study, the lack of details on storage are unlikely to have a substantial impact on the study results.
Met	tric 8:	Consistency of Exposure Administration	Low	The exposure volume (0.5mL) was reported, but due to deficiencies in reporting details about the controls, it is unclear if control animals were administered a consistent volume of the vehicle.
Met	tric 9:	Reporting of Doses/Concentrations	Medium	A mg/kg dose can be estimated based on the information provided.
Met	tric 10:	Exposure Frequency and Duration	Medium	No details justifying the exposure frequency or duration were provided, although the single oral dose appeared to be appropriate for examining the outcomes of interest.
Met	tric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The study authors did not justify the use of a single exposure group; additional groups would have been more appropriate for identifying a dose-response.
Met	tric 12:	Exposure Route and Method	High	The exposure route and method were appropriate for the test substance.
Domain 4: Test Animals				
	tric 13:	Test Animal Characteristics	Low	Animal species, sex, and starting body weights were reported. Strain, age, and source were not specified.
Met	tric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported to evaluate if husbandry was adequate and whether differences occurred between control and exposed populations. These deficiencies are likely to have a substantial impact on results.

## Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Natsyuk, M. V., Chekman, I. S. (1975). Content of nicotinamide coenzymes in liver and myocardium of rats poisoned with dichloroethane. Bulletin of

Experimental Biology and Medicine 79(4):408-409.

Health

Mortality

Outcome(s): Reported Health

Mortality

Effect(s): Duration:

Chemical:

Acute (less than or equal to 24 hr) Single gavage 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 5441424

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group (14-16) was sufficient.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Details of outcome assessment were not reported; however, there is not a substantial impact on results for this outcome.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding the execution of the study protocol for outcome assessment were not reported. This is unlikely to have a a substantial impact on results for this outcome of interest.
	Metric 18:	Sampling Adequacy	High	All of the animals were evaluated for this outcome.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome of interest.
	Metric 20:	Negative Control Response	Low	The biological response of the negative control groups were not reported.
D : ( C f	r /W : 11 C	. 1		
Domain 6: Confound			_	
	Metric 21:	Confounding Variables in Test Design	Low	Body weights were not measured.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was not performed for this outcome; but could be performed based on the information provided.
	Metric 24:	Reporting of Data	Low	Results for the treatment group were described in the text. The negative control results were not explicitly reported, but can be gleaned based on the No. of rats sampled for other endpoints.

# **Overall Quality Determination**

Low

Natsyuk, M. V., Chekman, I. S. (1975). Content of nicotinamide coenzymes in liver and myocardium of rats poisoned with dichloroethane. Bulletin of

HERO ID: 5441424 Table: 2 of 2

**Study Citation:** 

Study Citation:		al Biology and Medicine 79(4):408-409.	omannue c	oenzymes in liver and myocardium of rats poisoned with dichloroethane. Bulletin o
Health		er; Cardiovascular;		
Outcome(s):	1	,		
Reported Health	Hepatic/Live	er: Nicotinamide coenzymes content in live	r; serum AL	T and AST, and histopathology; Cardiovascular: Nicotinamide coenzymes content i
Effect(s):		and histopathology;	,	
<b>Duration:</b>		han or equal to 24 hr) Single gavage		
Chemical:		pethane- Isomer: Dichloroethane		
HERO ID:	5441424			
Domain		Metric	Rating	Comments
Domain 1: Test Substar				
	Metric 1:	Test Substance Identity	Low	All Outcomes: The reported test substance was dichloroethane. The CASRN and source of the test substance were not provided to confirm its identity. Ambiguity and the inability to confirm the isomer used is likely to have a substantial impact on the study results.
	Metric 2:	Test Substance Source	Low	All Outcomes: The test substance source was not reported.
	Metric 3:	Test Substance Purity	Low	All Outcomes: The test substance purity was not reported.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: Negative controls were included, but the it was unclear whether the negative control was untreated vs. a vehicle control), and the lack of details is likely to have a substantial impact on results.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.
Domain 3: Exposure Cl	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The test substance was administered as a 20% solution in sunflower oil. Details on preparation were not provided. Information on storage was not reported, although due to the acute nature of the study, the lack of details on storage are unlikely to have a substantial impact on the study results.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: The exposure volume (0.5mL) was reported, but due to deficiencies in reporting details about the controls, it is unclear if control animals were administered a consistent volume of the vehicle.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: A mg/kg dose can be estimated based on the information provided.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: No details justifying the exposure frequency or duration were provided, although the single oral dose appeared to be appropriate for examining the outcomes of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The study authors did not justify the use of a single exposure group; additional groups would have been more appropriate for identifying a dose-response.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route and method were appropriate for the test substance.
Domain 4: Test Animal	S			
Domain 1. 10st / millian	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Animal species, sex, and starting body weights were reported. Strain, age, and source were not specified.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not sufficiently reported to evaluate if husbandry was adequate and whether differences occurred between control and exposed populations. These deficiencies are likely to have a substantial impact on results.
	<u> </u>	Conti	nued on nex	t naga

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		contin	ued from p	revious page			
Study Citation:		V., Chekman, I. S. (1975). Content of nic al Biology and Medicine 79(4):408-409.	otinamide c	oenzymes in liver and myocardium of rats poisoned with dichloroethane. Bulletin o			
Health	Hepatic/Live	er; Cardiovascular;					
Outcome(s):							
Reported Health			r; serum AL	T and AST, and histopathology; Cardiovascular: Nicotinamide coenzymes content i			
Effect(s):		and histopathology;					
Duration:		Acute (less than or equal to 24 hr) Single gavage					
Chemical:	,	oethane- Isomer: Dichloroethane					
HERO ID:	5441424						
Domain		Metric	Rating	Comments			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals per group (14-16) was sufficient.			
Domain 5: Outcome A	Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Details of the outcome assessment were not reported; the outcome assessment partially addressed the outcomes of interest - organ weights were not included. Histopathology was considered to be a sensitive measure for the outcomes of interest.			
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: There was incomplete reporting of the outcome assessment protocol execution and these deficiencies are likely to have a substantial impact on results.			
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Due to reporting deficiencies, sampling details were only available for some, but not all of the outcomes of interest.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this outcome of interest.			
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological response of the negative control groups was not reported for some of the outcomes of interest.			
Domain 6: Confoundi	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: Body weights were not measured.			
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	Low	All Outcomes: Statistical analysis was performed but not described adequately. It is unclear whether histopathology data were statistically analyzed and the data were not provided for independent review.			
	Metric 24:	Reporting of Data	Low	All Outcomes: Means with an unspecified measure of variance were provided for some endpoints. Histopathology data were described qualitatively in the text; incidences and responses in the control groups were not provided.			
Overall Qual	ity Deterr	nination	Low				

Human Health Hazard Animal Toxicology Evaluation HERO ID: 5441056 Table: 1 of 2

**Study Citation:** Natsyuk, M.V., Fedurov, V.V. (1974). Effect of methyluracil on oxidative phosphorylation in the hepatic mitochondria of rats poisoned with dichloroethane.

Bulletin of Experimental Biology and Medicine 77:391-393.

Health Mortality

**Outcome(s):** 

**Reported Health** Death

Effect(s):

**Duration:** 

Acute (less than or equal to 24 hr) Single oral gavage

Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
N	Metric 1:	Test Substance Identity	Low	The test substance was identified; however, there were uncertainties that are likely to have a substantial impact on the study results. The test substance was identified as dichloroethane, with no specification of the isomer and no CASRN or source provided.
N	Metric 2:	Test Substance Source	Low	The test substance source was not provided.
N	Metric 3:	Test Substance Purity	Low	The purity was not reported, and the test substance was administered as a 20% solution.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	Low	The study included a group of "intact" rats presumed to be the controls. The nature of these controls was not specified (e.g., untreated or vehicle controls), which is expected to substantially impact the study results.
N	Metric 5:	Positive Controls	N/A	A positive control group was not included, but are not required for this study type.
N	Metric 6:	Randomized Allocation of Animals	Low	The method of animal allocation into study groups was not specified.
Domain 3: Exposure Chara				
N	Metric 7:	Preparation and Storage of Test Substance	Low	Details of test substance preparation were not provided. It was indicated that the test substance was administered as a 20% solution in sunflower oil, but the lack of preparation details could have a significant impact on the study results. No information on storage was included in the study report; however, due to the acute nature of the study, this is not expected to substantially impact the study results.
N	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and the missing information is likely to have a substantial impact on results. Test animals were administered a gavage volume of 0.5 mL/kg which was not considered excessive. It was not reported whether control animals were consistently dosed.
N	Metric 9:	Reporting of Doses/Concentrations	Medium	Animals were administered 0.5 mL/kg of a 20% dichloroethane solution. Dosing in mg/kg was not specified, but assuming 20% is equivalent to 200 mg/L, the animals were administered a 100 mg/kg dose. There was no mention of analytical verification of the concentration of the test substance in the solution.
N	Metric 10:	Exposure Frequency and Duration	Medium	Animals were administered a single dose via gavage. The study authors did not justify their dosing methods, including the frequency and duration, but the single dose appeared to be appropriate for the purposes of the study.
			Continued on next page	

Study Citation: Natsyuk, M.V., Fedurov, V.V. (1974). Effect of methyluracil on oxidative phosphorylation in the hepatic mitochondria of rats poisoned with dichloroethane.

Bulletin of Experimental Biology and Medicine 77:391-393.

Health

Mortality

**Outcome(s):** 

Reported Health

Death

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single oral gavage

**Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

HERO ID.	3441030			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The purposes of the study were to evaluate the potential therapeutic effects of methyluracil in animals "poisoned" with dichloroethane. The study was not focused on determining a dose-response of the test substance, and dichloroethane was being used as a chlorinated hydrocarbon known to cause mitochondrial damage to hepatocytes. However, the authors did not justify the single dose used.
	Metric 12:	Exposure Route and Method	High	Gavage was an appropriate route of exposure for the test substance and this study.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	Limited details of the test animals were provided. Only the sex, species (male rats), and initial body weight range were reported. The source and strain were not specified.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	No animal husbandry conditions were described and it is unclear whether husbandry conditions were adequate and consistent across groups. These deficiencies are likely to have a substantial impact on results.
	Metric 15:	Number of Animals per Group	Low	The number of animals per group was not clearly reported. The study noted that 72 animals were used in total, and in the results descriptions indicated that 36 rats were "poisoned" with the test material. The number of rats in the control group was not specified.
Domain 5: Outcome Ass	essment			
	Metric 16:	Outcome Assessment Methodology	Medium	The methods did not indicate that animals were observed for mortality. The number of deaths was reported in the results indicating this as a study endpoint.
	Metric 17:	Consistency of Outcome Assessment	Medium	Limited details of outcome assessment were provided. The times of sacrifice were clearly reported. There is no indication that observations of mortality were different across groups.
	Metric 18:	Sampling Adequacy	Medium	Sampling was not described for this endpoint, but based on the available text, it is assumed that all animals were observed for mortality.
	Metric 19:	Blinding of Assessors	N/A	The use of blinding in the study was not specified, but blinding is not necessary for a mortality endpoint
	Metric 20:	Negative Control Response	Low	The negative control responses were not reported.
Domain 6: Confounding	/ Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report information to determine confounding (e.g., animal husbandry conditions, body weights), but the reported information did not identify any differences across groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	The number of animals that died in the treatment group was high. No further information was provided, and deaths in the control group were not reported, so it is unclear whether any deaths were due to health outcomes that were unrelated to exposure.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 5441056 Table: 1 of 2

## ... continued from previous page

**Study Citation:** Natsyuk, M.V., Fedurov, V.V. (1974). Effect of methyluracil on oxidative phosphorylation in the hepatic mitochondria of rats poisoned with dichloroethane.

Bulletin of Experimental Biology and Medicine 77:391-393.

Health

**Outcome(s):** 

Death

Mortality

**Reported Health** 

Effect(s): Acute (less than or equal to 24 hr) Single oral gavage **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 5441056

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Uninformative	It is not clear whether statistical analysis was performed on mortality data, and the data for the control group were not provided, precluding the ability to perform an independent analysis.
	Metric 24:	Reporting of Data	Low	Mortality incidences were reported for the treatment group, but not for the controls, and the text did not explicitly specify that no control animals died.

# **Overall Quality Determination**

# Uninformative

Study Citation: Natsyuk, M.V., Fedurov, V.V. (1974). Effect of methyluracil on oxidative phosphorylation in the hepatic mitochondria of rats poisoned with dichloroethane.

Bulletin of Experimental Biology and Medicine 77:391-393.

Health

Hepatic/Liver

Outcome(s): Reported Health

Serum ALT, hippuric acid in the urine, and respiration and phosphorylation in liver mitochondria

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Single oral gavage

**Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	Low	The test substance was identified; however, there were uncertainties that are likely to have a substantial impact on the study results. The test substance was identified as dichloroethane, with no specification of the isomer and no CASRN or source provided.
	Metric 2:	Test Substance Source	Low	The test substance source was not provided.
	Metric 3:	Test Substance Purity	Low	The purity was not reported, and the test substance was administered as a 20% solution.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	Low	The study included a group of "intact" rats presumed to be the controls. The nature of these controls was not specified (e.g., untreated or vehicle controls), which is expected to substantially impact the study results.
	Metric 5:	Positive Controls	N/A	A positive control group was not included, but are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	The method of animal allocation into study groups was not specified.
Domain 3: Exposure Ch	naracterization Metric 7:	Preparation and Storage of Test Substance	Low	Details of test substance preparation were not provided. It was indicated that the test substance was administered as a 20% solution in sunflower oil, but the lack of preparation details could have a significant impact on the study results. No information on storage was included in the study report; however, due to the acute nature of the study, this is not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and the missing information is likely to have a substantial impact on results. Test animals were administered a gavage volume of 0.5 mL/kg which was not considered excessive. It was not reported whether control animals were consistently dosed.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Animals were administered 0.5 mL/kg of a 20% dichloroethane solution. Dosing in mg/kg was not specified, but assuming 20% is equivalent to 200 mg/L, the animals were administered a 100 mg/kg dose. There was no mention of analytical verification of the concentration of the test substance in the solution.
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were administered a single dose via gavage. The study authors did not justify their dosing methods, including the frequency and duration, but the single dose appeared to be appropriate for the purposes of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The purposes of the study were to evaluate the potential therapeutic effects of methyluracil in animals "poisoned" with dichloroethane. The study was not focused on determining a dose-response of the test substance, and dichloroethane was being used as a chlorinated hydrocarbon known to cause mitochondrial damage to hepatocytes. However, the authors did not justify the single dose used.
	Metric 12:	Exposure Route and Method	High	Gavage was an appropriate route of exposure for the test substance and this study.

# Human Health Hazard Animal Toxicology Evaluation

## ... continued from previous page

Study Citation: Natsyuk, M.V., Fedurov, V.V. (1974). Effect of methyluracil on oxidative phosphorylation in the hepatic mitochondria of rats poisoned with dichloroethane. Bulletin of Experimental Biology and Medicine 77:391-393.

Health

Hepatic/Liver

Outcome(s): Reported Health

Serum ALT, hippuric acid in the urine, and respiration and phosphorylation in liver mitochondria

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Single oral gavage

**Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 5441056

HERO ID:	5441056			
Domain		Metric	Rating	Comments
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Low	Limited details of the test animals were provided. Only the sex, species (male rats), and initial body weight range were reported. The source and strain were not specified.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	No animal husbandry conditions were described and it is unclear whether husbandry conditions were adequate and consistent across groups. These deficiencies are likely to have a substantial impact on results.
	Metric 15:	Number of Animals per Group	Low	The number of animals per group was not clearly reported. The study noted that 72 animals were used in total, and in the results descriptions indicated that 36 rats were "poisoned" with the test material. The number of rats in the control group was not specified.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Details of the outcome assessment methodology were limited or referenced to other studies. One of the referenced studies is in Russian, and the citation for the second referenced study is incomplete. The outcomes assessed were focused on the liver, particularly changes in oxidative phosphorylation. Standard endpoints for evaluating liver toxicity (e.g., organ weights, histopathology), were not included.
	Metric 17:	Consistency of Outcome Assessment	Medium	Limited details of outcome assessment were provided. The times of sacrifice were clearly reported. Details of the timing of urine collection were not provided. Based on the available information, there is no indication of inconsistencies across groups.
	Metric 18:	Sampling Adequacy	Medium	Sampling was not reported for most endpoints (e.g., serum chemistry, and urine measurements). For measurements of oxidative phosphorylation, 8 animals per time point were used, which was sufficient.
	Metric 19:	Blinding of Assessors	N/A	The use of blinding in the study was not specified, but blinding is not necessary for the endpoints described (serum chemistry, urinalysis, mitochondrial function).
	Metric 20:	Negative Control Response	Medium	Values of the negative control response were reported for all of the outcomes specified, although not at each time point (ALT, hippuric acid); the reported responses appeared to be adequate.
Domain 6: Confoundin	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report information to determine confounding (e.g., animal husbandry conditions, body weights), but the reported information did not identify any differences across groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	The number of animals that died in the treatment group was high. No further information was provided, and deaths in the control group were not reported, so it is unclear whether any deaths were due to health outcomes that were unrelated to exposure.

HERO ID: 5441056 Table: 2 of 2

1,1-Dichloroethane

## ... continued from previous page

Study Citation: Natsyuk, M.V., Fedurov, V.V. (1974). Effect of methyluracil on oxidative phosphorylation in the hepatic mitochondria of rats poisoned with dichloroethane.

Bulletin of Experimental Biology and Medicine 77:391-393.

Health

Hepatic/Liver

**Outcome(s):** 

Reported Health

Serum ALT, hippuric acid in the urine, and respiration and phosphorylation in liver mitochondria

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Single oral gavage

**Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 5441056

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Low	Based on the study text, some statistical analysis was conducted, but the methods used were not clearly described.
	Metric 24:	Reporting of Data	Low	Data for some endpoints were inadequately reported. Serum ALT and hippuric results were not clearly reported at each time point for the control group. Measures of variance were provided but were not clearly defined. For example, data are reported to be "M $\pm$ m".

# **Overall Quality Determination**

Low

HERO ID: 5441619 Table: 1 of 1

**Study Citation:** 

Sergeev, S. N., Berezhnoi, R. V. (1977). Changes in distribution of carbonic-anhydrase activity in rat myocardium and liver during acute dichloroethane

poisoning (histophotometric investigation). Bulletin of Experimental Biology and Medicine 83:108-110.

Health

Mortality

**Outcome(s):** 

Reported Health

Mortality

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single gavage **Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 

5441619

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	Low	Test substance was identified only as dichloroethane. It is unclear if it is 1,1-dichloroethane, 1,2-dichlorethane, or possibly a mixture. The CASRN is not specified resulting in uncertainty.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	Purity or grade were not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Low	A control rat was sacrificed and examined with each exposed animal when it died or was sacrificed; however, it is not clear if control animals were administered a vehicle or were untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Test substance preparation and storage were not fully described. Given the volatility of the test substance, lack of reporting storage conditions and timing from when solution was made until use, could substantially impact results.
	Metric 8:	Consistency of Exposure Administration	Low	Animals were administered a gavage volume of 1 ml, however doses were made for eac animal individually adding potential for inconsistencies in dose delivered.
	Metric 9:	Reporting of Doses/Concentrations	Low	Doses were not adequately reported. Doses were reported as a range of volumes. Body weights were not reported for this oral gavage study. Lack of reporting is likely to substantially impacting results.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The number of exposure groups were not provided. Study reports doses as a range with total numbers of animals used; but does not provide any other information. It cannot be determined how may exposure group there were.
	Metric 12:	Exposure Route and Method	Low	The route (gavage) was appropriate for test substance.
Domain 4: Test Animals	s			
20mm ii 1000 mmman	Metric 13:	Test Animal Characteristics	Low	The source or sex of the test animal was not reported. These deficiencies are likely to have a substantial impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
		Con	ntinued on next page .	

Study Citation: Sergeev, S. N., Berezhnoi, R. V. (1977). Changes in distribution of carbonic-anhydrase activity in rat myocardium and liver during acute dichloroethane

poisoning (histophotometric investigation). Bulletin of Experimental Biology and Medicine 83:108-110.

**Health** Mortality

Outcome(s):

Reported Health

Reported Health Effect(s):

Mortality

**Duration:** Chemical:

Acute (less than or equal to 24 hr) Single gavage 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 5441619

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	The number of animals/group was not reported.
D : 5.0.4				
Domain 5: Outcome				
	Metric 16:	Outcome Assessment Methodology	Low	Study reported on death of animals after dosing but does not provide details on timing of assessment.
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding execution of protocol are not reported. It is not reported how often animals were checked on, or if moribund animals were sacrificed early.
	Metric 18:	Sampling Adequacy	Low	Sampling was not adequately reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for mortality.
	Metric 20:	Negative Control Response	Low	It is not reported in any control animals died.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report all information to determine confounding. Body weight, food intake or clinical observations were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Uninformative	Statistical analysis was not performed. The study evaluated death; however, number of animals per group are not reported.
	Metric 24:	Reporting of Data	Uninformative	Data were not reported adequately. The study reports all animals in the high dose group died within 15 minutes but does not report how many animals were studied. All other animals died within 2 days, but again, no details or numbers are provided.

# **Overall Quality Determination**

## Uninformative

Zabrodskii, P.F., Germanchuk, V.G., Kirichuk, V.F., Nodel', M.L., Aredakov, A.N. (2003). Anticholinesterase mechanism as a factor of immunotoxicity of

HERO ID: 1776866 Table: 1 of 1

	-		
1	1	Dich	loroethane

**Study Citation:** 

Health	various chemical compounds. Bulletin of Experimental Biology and Medicine 136(2):176-178.  Sensitization: Immune/Hematological:							
Outcome(s): Reported Health Effect(s):  Duration: Chemical: HERO ID:	Sensitization; Immune/Hematological;  Sensitization: Administration of dichloroethane significantly (p<0.05) decreased delayed-type hypersensitivity (DTH) reaction in rats 4 days after treatment (measured by increase in hind paw weight, 18.9% with DCE vs. 27.8% in controls, i.e., a decrease of 1.47 times; Table 1).; Immune/Hematological: Mechanistic effects on immune parameters; Mechanistic: Administration of dichloroethane significantly (p<0.05) decreased acetylcholinesterase (ACE) activity in T lymphocytes in the spleen, compared to controls, 4 days after treatment (Table 1). Dichloroethane treatment also significantly (p<0.05) decreased the number of antibody-producing cells (APC) in splenic T lymphocytes 4 days after treatment (Table 1). Dichloroethane also decreased the counts of α-naphthyl-AS-acetate esterase-positive cells (T cells, 1.20 times) and α-naphthylbutyrate esterase-positive T lymphocytes (1.21 times) in the spleen, but the results were not statistically significant (i.e., p>0.05, Table 2).;  Acute (less than or equal to 24 hr) Acute (single subcutaneous injection)  1,1-Dichloroethane- Isomer: Dichloroethane  1776866							
Domain		Metric	Rating	Comments				
Domain 1: Test Substan	ce Metric 1:	Test Substance Identity	Uninformative	All Outcomes: The test substance was identified only as dichloroethane. The isomer being administered is not reported. No CAS No. is provided.				
	Metric 2:	Test Substance Source	Low	All Outcomes: The source was not reported and the test substance identity was not analytically verified by the testing laboratory.				
	Metric 3:	Test Substance Purity	Low	All Outcomes: Purity and/or grade of test substance were not reported.				
Domain 2: Test Design								
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: Details regarding the negative control group were not reported and it is unclear whether the negative control was untreated vs. a vehicle control.				
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for this study type				
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.				
Domain 3: Exposure Ch	aracterization							
Bomain 5. Exposure Cir	Metric 7:	Preparation and Storage of Test Substance	Low	Sensitization: No information on preparation or storage of test substance was provided, and lack of details could substantially impact results since the test substance is potentially volatile.; Immune/Hematological: No information on preparation or storage of test substance was provided, and lack of details could substantially impact results since the test substance is potentially volatile				
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported (i.e., injection volume was not reported) and the missing information is likely to have a substantial impact on results.				
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	All Outcomes: Test animals were administered a single dose equivalent to 0.75% the LD50. No additional information was provided and the administered dose was not reported.				
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The test substance was administered as a single subcutaneous dose. This is appropriate for an acute study.				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: A single dose group was included in the study. Study authors do not justify the selected dose.				
		Cor	ntinued on next page .					

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Sensitization; Immune/Hematological;						
Sensitization	n: Administration of dichloroethane significantly	(p<0.05) decreased	delayed-type hypersensitivity (DTH) reaction in rats 4 days after treatment			
(measured b	y increase in hind paw weight, 18.9% with Do	CE vs. 27.8% in co	ontrols, i.e., a decrease of 1.47 times; Table 1).; Immune/Hematological:			
Mechanistic	effects on immune parameters; Mechanistic: A	Administration of dic	chloroethane significantly (p<0.05) decreased acetylcholinesterase (ACE)			
•		,				
			d $\alpha$ -naphthylbutyrate esterase-positive T lymphocytes (1.21 times) in the			
spleen, but the	he results were not statistically significant (i.e., j	p>0.05, Table 2).;				
		us injection)				
1776866	semane isomer. Bemoreculaire					
	Metric	Rating	Comments			
Metric 12:			All Outcomes: The test substance was administered as a single subcutaneous injection.			
	¥		,			
ls		_				
Metric 13:	Test Animal Characteristics	Low	All Outcomes: "Experiments were carried out on male Wistar rats (180-220 g)." The source of the animals and animal age was not reported.			
Metric 14:	Adequacy and Consistency of Animal	Low	All Outcomes: Husbandry conditions were not sufficiently reported to evaluate if hus-			
	Husbandry Conditions		bandry was adequate and whether differences occurred between control and exposed groups.			
Metric 15:	Number of Animals per Group	Medium	All Outcomes: 9-11 animals were included per group. This is appropriate for an acute duration study.			
ggaggmant						
	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended out-			
wiettie 10.	Outcome Assessment Wednodology	Ingn	come(s) of interest.			
Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.			
Metric 18:	Sampling Adequacy	High	All Outcomes: All treated animals were sampled for the outcomes of interest.			
Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcomes being assessed.			
Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control groups appear adequate			
a / Variabla Car	mtun.l					
-		Medium	All Outcomes: Although the study did not report all information to determine confound			
Wieure 21.	and Procedures	Wedium	ing, reported information did not identify differences among study groups in confounding measures.			
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion the there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.			
Metric 23:	Data Presentation and Analysis	Low	All Outcomes: Student's t-test used and analysis is not adequately described; unclear if appropriate for data set since t tests are parametric and normal distribution was not shown; however, means with deviations are provided to allow an independent analysis.			
		tinued on next page				
	various cher Sensitization Sensitization (measured be Mechanistic activity in Telegraph decreased the counts of α-spleen, but the Acute (less to 1,1-Dichloro 1776866)  Metric 12:  Is Metric 13: Metric 14: Metric 15:  Sessessment Metric 16: Metric 17: Metric 18: Metric 19: Metric 19: Metric 20:  g / Variable Cometric 21:  Metric 22:	various chemical compounds. Bulletin of Experimental Biol Sensitization; Immune/Hematological;  Sensitization: Administration of dichloroethane significantly (measured by increase in hind paw weight, 18.9% with Dimension Mechanistic effects on immune parameters; Mechanistic: A activity in T lymphocytes in the spleen, compared to cont decreased the number of antibody-producing cells (APC) in counts of α-naphthyl-AS-acetate esterase-positive cells (T spleen, but the results were not statistically significant (i.e., Acute (less than or equal to 24 hr) Acute (single subcutaneon 1,1-Dichloroethane-Isomer: Dichloroethane 1776866  Metric  Metric 12: Exposure Route and Method  Sometric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group  Sesessment Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure	Sensitization: Administration of dichloroethane significantly (p<0.05) decreased (measured by increase in hind paw weight, 18.9% with DCE vs. 27.8% in co Mechanistic effects on immune parameters; Mechanistic: Administration of dic activity in T lymphocytes in the spleen, compared to controls, 4 days after tr decreased the number of antibody-producing cells (APC) in splenic T lymphoc counts of α-naphthyl-AS-acetate esterase-positive cells (T cells, 1.20 times) an spleen, but the results were not statistically significant (i.e., p>0.05, Table 2).; Acute (less than or equal to 24 hr) Acute (single subcutaneous injection) 1,1-Dichloroethane- Isomer: Dichloroethane 1776866  Metric Rating  Metric 12: Exposure Route and Method High  Metric 13: Test Animal Characteristics Low  Metric 14: Adequacy and Consistency of Animal Low  Husbandry Conditions  Metric 15: Number of Animals per Group Medium  ssessment  Metric 16: Outcome Assessment Methodology High  Metric 17: Consistency of Outcome Assessment High  Metric 18: Sampling Adequacy High  Metric 19: Blinding of Assessors N/A  Metric 20: Negative Control Response High  g / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Medium  Exposure			

HERO ID: 1776866 Table: 1 of 1

... continued from previous page

Study Citation: Zabrodskii, P.F., Germanchuk, V.G., Kirichuk, V.F., Nodel', M.L., Aredakov, A.N. (2003). Anticholinesterase mechanism as a factor of immunotoxicity of

various chemical compounds. Bulletin of Experimental Biology and Medicine 136(2):176-178.

**Health** Sensitization; Immune/Hematological;

**Outcome(s):** 

Reported Health Effect(s):

Sensitization: Administration of dichloroethane significantly (p<0.05) decreased delayed-type hypersensitivity (DTH) reaction in rats 4 days after treatment (measured by increase in hind paw weight, 18.9% with DCE vs. 27.8% in controls, i.e., a decrease of 1.47 times; Table 1).; Immune/Hematological:

Mechanistic effects on immune parameters; Mechanistic: Administration of dichloroethane significantly (p<0.05) decreased acetylcholinesterase (ACE) activity in T lymphocytes in the spleen, compared to controls, 4 days after treatment (Table 1). Dichloroethane treatment also significantly (p<0.05) decreased the number of antibody-producing cells (APC) in splenic T lymphocytes 4 days after treatment (Table 1). Dichloroethane also decreased the counts of  $\alpha$ -naphthyl-AS-acetate esterase-positive cells (T cells, 1.20 times) and  $\alpha$ -naphthylbutyrate esterase-positive T lymphocytes (1.21 times) in the

spleen, but the results were not statistically significant (i.e., p>0.05, Table 2).;

**Duration:** 

Acute (less than or equal to 24 hr) Acute (single subcutaneous injection)

**Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 1776866

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	High	All Outcomes: Data are sufficiently reported for all outcomes of interest by exposure
				group.

## **Overall Quality Determination**

## Uninformative

Study Citation:	Zabrodskii, P.F., Troshkin, N.M., Mandych, V.G. (2004). Stimulation of immunotoxicity of chemicals metabolizing in vivo into highly toxic compounds
	by the monooxygenase system inductors. Bulletin of Experimental Biology and Medicine 138(4):369-371.
Health	Immune/Hematological

**Outcome(s):** 

Reported Health Effect(s):

Humoral immune reaction to T-dependent (sheep erythrocytes) and T-independent (typhoid fever Vi antigen) antigens; activity of natural killer cells;

antibody-dependent cell cytotoxicity and delayed type hypersensitivity.

**Duration:** Acute (less than or equal to 24 hr) nan **Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane **HERO ID:** 1048005

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	Low	Test substance was identified as dichloroethane, however, no information was provided on the isomer composition, which could have an impact on hazard properties.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design	ı			
	Metric 4:	Negative and Vehicle Controls	Low	The negative control group was included but details were not provided (vehicle or untreated).
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure C	haracterization			
Bonium 3. Exposure e	Metric 7:	Preparation and Storage of Test Substance	Low	Test substance preparation and storage were not adequately described given the volatility of the test substance, however, the study is an acute dose study and therefore, the lack of details is unlikely to have a substantial impact on results.
	Metric 8:	Consistency of Exposure	Low	The gavage volume was not reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	Only nominal doses were reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were reported and appropriate for this study.
	Metric 11:	Number of Exposure Groups and	Low	A NOAEL was not obtained. The dose studied was the LD50.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	Low	Vehicle not reported.
Domain 4: Test Anima	ls			
Domain 1. Test I minu	Metric 13:	Test Animal Characteristics	Low	The source of test animals was not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were adequately reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Low	The number of animals per study group was not reported.
Domain 5: Outcome A	ssessment			
Domain J. Outcome A	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate (n=6-10).
			ued on next pa	

Study Citation: Zabrodskii, P.F., Troshkin, N.M., Mandych, V.G. (2004). Stimulation of immunotoxicity of chemicals metabolizing in vivo into highly toxic compounds by the monooxygenase system inductors. Bulletin of Experimental Biology and Medicine 138(4):369-371.

Health

Immune/Hematological

Outcome(s): Reported Health

Humoral immune reaction to T-dependent (sheep erythrocytes) and T-independent (typhoid fever Vi antigen) antigens; activity of natural killer cells; antibody-dependent cell cytotoxicity and delayed type hypersensitivity.

Effect(s):
Duration:
Chemical:

Acute (less than or equal to 24 hr) nan 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 1048005

Domain	Metric	Rating	Comments
Metric 1	9: Blinding of Assessors	N/A	Blinding was not necessary.
Metric 2	): Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable Metric 2		Medium	Although the study did not report all information to determine confounding, reported information did not identify differences.
Metric 2		Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Metric 2	1	High	Statistical analysis was appropriate.
Metric 2	Reporting of Data	High	Data were fully reported.

# **Overall Quality Determination**

# Medium

Study Citation: Ghanayem, B. I., Maronpot, R. R., Matthews, H. B. (1986). Association of chemically induced forestomach cell proliferation and carcinogenesis. Cancer

Letters 32(3):271-278.

**Health** Gastrointestinal

**Outcome(s):** 

**Reported Health** Forestomach cell proliferation

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 2 weeks - Dichloroethane **Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 11728

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	Low	The test substance was identified as dichloroethane; no CASRN or structure was provided. However, the study points to previous results using the same chemical; this study identifies the test substance as 1,1-dichloroethane. Dichloroethane was selected as an isomer of 1,1-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was specified; the source (National Toxicology Program chemical repository) was not a manufacturer; a batch/lot number was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
20 1000 2 000gu	Metric 4:	Negative and Vehicle Controls	High	A negative vehicle-only (corn oil) control group was used; it was indicated that the same protocol was used for treated rats and controls.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type; effects on forestomach proliferation were observed in the study, indicating that the study (as performed) was able to detect a positive response.
	Metric 6:	Randomized Allocation of Animals	Low	The methods by which animals were allocated to study groups was not reported.
Domain 3: Exposure Ch	aracterization			
Donam 3. Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Low	Other than indicating that the test substance was dissolved in corn oil, no details on preparation or storage was reported. Because the test substance is volatile, the lack of preparation/storage information has the potential to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Low	It was indicated that dose volumes were the same as those used in a previous carcinogenicity assay. Based on review of that reference (HEROID 646679), gavage volumes were not specified.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were explicitly reported and appeared adequate for the outcome of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The doses used were based on a previous carcinogenicity study; it was not entirely clear if the high dose was high enough to detect a response (the high dose was considered a NOAEL; the duration of the study was shorter than in the previous carcinogenicity study).
	Metric 12:	Exposure Route and Method	High	The route (oral) and method (gavage) of administration were reported (the same as the previous carcinogenicity study) and were suited to the (volatile) test substance.

Study Citation: Ghanayem, B. I., Maronpot, R. R., Matthews, H. B. (1986). Association of chemically induced forestomach cell proliferation and carcinogenesis. Cancer

Letters 32(3):271-278.

**Health** Gastrointestinal

**Outcome(s):** 

**Reported Health** 

Forestomach cell proliferation

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 2 weeks - Dichloroethane **Chemical:** 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 11728

Domain		Metric	Rating	Comments
Domain 4: Test Anir	nals			
	Metric 13:	Test Animal Characteristics	Medium	The age of the rats was not reported. The species, strain, sex, and starting body weights (as a range) were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions, included temperature, humidity, light-dark cycle, diet, and water availability were reported; these conditions appeared to apply to both control and exposed groups. The number of animals per cage was not indicated.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group (8-16) was adequate for the study type, and was sufficient for statistical analysis.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The methods used (histology) were adequate to detect the outcome of interest (forestom ach proliferation and/or hyperkeratosis).
	Metric 17:	Consistency of Outcome Assessment	High	The outcome was assessed consistently across groups (i.e., 24 hours after administration of the last dose).
	Metric 18:	Sampling Adequacy	High	Histological evaluations were performed on all animals.
	Metric 19:	Blinding of Assessors	High	Blinding was explicitly reported; histological samples were evaluated by pathologists with no knowledge of treatment.
	Metric 20:	Negative Control Response	High	There was no evidence of forestomach cell proliferation or hyperkeratosis in control rats.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not all report information to determine confounding; however, the nature of the study (i.e., 2 week study evaluating histology) suggests that any differences among groups would not likely impact the study results.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information regarding differences among groups in animal attrition or outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	The study compared the incidence of forestomach lesions in treated animals to controls using a one-sided Fischer exact test. However, the incidence of lesions in controls and dichloroethane-treated animals was 0; statistical analyses were not required.
	Metric 24:	Reporting of Data	High	Data for the incidence of forestomach cell proliferation and hyperkeratosis were reported for controls and both groups of dichloroethane-treated animals.

# **Overall Quality Determination**

## Medium

Study Citation:	Vozovaia, M.A. (1977). [The effect of dichloroethane on the sexual cycle and embryogenesis of experimental animals]. Akusherstvo i Ginekologiya
	2(2):57-59.
Health	Immune/Hematological; Hepatic/Liver; Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Mortality; Nutritional/Metabolic;
Outcome(s):	
Reported Health	Immune/Hematological: Leukoctye concentration and phagocytic activity; Hepatic/Liver: Functional tests, possibly liver weight; Reproduc-
Effect(s):	tive/Developmental: Estrous cycle parameters, pathology of reproductive organs, mating and fertility, and/or fetal development; Musculoskeletal: Func-
	tional tests for muscular activity (the summation-threshold index, the effect of angular acceleration, the Quick-Pytel test, the swim test, etc.); Neurologi-

**Duration:** Chemical: cal/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights; Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane

1,1-Dichloroethane- Isomer: Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ance			
	Metric 1:	Test Substance Identity	Low	All Outcomes: The test substance was identified as dichloroethane (indicated in the PECO as an isomer of 1,1-dichloroethane).
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was not reported and was not analytically verified.
	Metric 3:	Test Substance Purity	Low	All Outcomes: Purity/test grade of the test substance was not reported.
Domain 2: Test Design	n			
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: The use of a concurrent negative control group was indicated; however, few to no details were provided (not indicated to be sham-treated). The control group was not exposed during the 4 months preceding pregnancy or during gestation.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The manner by which animals were allocated to study groups was not reported.
Domain 3: Exposure C	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Storage and preparation of the volatile test substance were not reported and there was no mention of the method or equipment used to generate the test substance.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration were insufficiently reported. No information on chamber designs or animals/chamber was provided.
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Actual or analytical concentrations were not reported. The concentration of 15 mg/m3 was selected as the "allowable limit." Although the concentration used was low, the study authors reported that developmental effects were observed.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: In the first part of the experiment, exposures were 4 hours/day, 6 days/week for 4 months. Rats were presumably exposed for 6 days during mating; half of the pregnant females were exposed for the "entire pregnancy" prior to sacrifice on GDs 17-19 (likely exposed daily). Dosing for 4 months prior to mating and gestation is an atypical study design.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: The study utilized controls and one concentration of dichloroethane. The study reported that effects development were observed at this dose, without evidence of maternal toxicity. Because only one dose was used, the study is not useful for doseresponse (i.e., both a NOAEL and a LOAEL could not be identified).

All Outcomes: The source of the test animals was not reported; sex and starting body weights were also not reported. Rats used in the study were mature, female, white rats;

#### ... continued from previous page

Study Citation: Vozovaia, M.A. (1977). [The effect of dichloroethane on the sexual cycle and embryogenesis of experimental animals]. Akusherstvo i Ginekologiya 2(2):57-59.

Health Immune/Hematological; Hepatic/Liver; Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Mortality; Nutritional/Metabolic;

Outcome(s): Reported Health

Effect(s):

Immune/Hematological: Leukoctye concentration and phagocytic activity; Hepatic/Liver: Functional tests, possibly liver weight; Reproductive/Developmental: Estrous cycle parameters, pathology of reproductive organs, mating and fertility, and/or fetal development; Musculoskeletal: Functional tests for muscular activity (the summation-threshold index, the effect of angular acceleration, the Quick–Pytel test, the swim test, etc.); Neurologi-

cal/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights;

Duration: Chemical: HERO ID: Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane 1.1-Dichloroethane- Isomer: Dichloroethane

62623

**Test Animal Characteristics** 

Metric 13:

Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Uninformative	All Outcomes: The method of exposure (i.e., whole-body or nose-only, static or dynamic) was not reported, neither was the number of air changes. There was no description of the air chamber.
Domain 4: Test Anima	ıls			

Low

however, they were non-pedigreed and were not likely the best choice for the study.

Metric 14: Adequacy and Consistency of Animal Husbandry Conditions

Metric 15: Number of Animals per Group

Low
All Outcomes: No husbandry conditions were not reported; these conditions have the potential to substantially the impact the study results.

All Outcomes: The number of animals per study group was not reported. 63 rats were used in total. The number of animals used to evaluate developmental effects (after gestational exposure) was presumably smaller than for the 4 month studies (half of the pregnant animals with 4 months pre-exposure continued exposure during pregnancy, and half did not).

Domain 5: Outcome Assessment

**Study Citation:** Vozovaia, M.A. (1977). [The effect of dichloroethane on the sexual cycle and embryogenesis of experimental animals]. Akusherstvo i Ginekologiya 2(2):57-59.

Health

**Outcome(s):** 

Reported Health Effect(s):

Immune/Hematological: Leukoctye concentration and phagocytic activity; Hepatic/Liver: Functional tests, possibly liver weight; Reproductive/Developmental: Estrous cycle parameters, pathology of reproductive organs, mating and fertility, and/or fetal development; Musculoskeletal: Functional tests for muscular activity (the summation-threshold index, the effect of angular acceleration, the Quick–Pytel test, the swim test, etc.); Neurologi-

Immune/Hematological; Hepatic/Liver; Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Mortality; Nutritional/Metabolic;

HERO ID: 62623 Table: 1 of 1

posed for 4 months and/or during gestation to evaluate systemic effects (body weights).

cal/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights; Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane

Duration: Chemical:

1.1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 62623

HERO ID.	02023			
Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Low	Immune/Hematological: Details about the outcome assessment were sparse. Animals were exposed for 4 months to evaluate immune effects (numbers of leukocytes and their phagocytic activity); rats were also evaluated for these effects during gestational exposure.; Hepatic/Liver: Details about the outcome assessment were sparse. The tests used to determine liver toxicity were not specified; it was not possible to evaluate if the tests were sensitive to the outcome of interest. It was not clear if liver effects were evaluated only during the 4 month exposure period, or also during gestation.; Reproductive/Developmental: Details about the outcome assessment were sparse. Animals were exposed for 4 months to evaluate estrous cycle effects, reproductive organ pathology, and systemic parameters; subsequent exposure (or no exposure) during gestation was performed to determine if effects on development were due to exposure before or during pregnancy.; Musculoskeletal: Details about the outcome assessment were sparse. The tests used to determine muscular activity were not explicitly specified (not possible to determine if outcome assessment was sensitive). It was not clear if muscular activity was evaluated as part of neurological tests. It was also not clear if these effects were evaluated only during the 4 month exposure period, or also during gestation.; Neurological/Behavioral: Details about the outcome assessment were sparse. Animals were exposed for 4 months to evaluate neurological effects; it was not entirely clear if rats were evaluated for these effects after gestational exposure as well.; Mortality: Details about the outcome assessment were sparse. Animals were presumably evaluated for mortality during both phases of the experiment (4 months, gestational exposure).; Nutritional/Metabolic: Details about the outcome assessment were sparse. Animals were ex-

Study Citation:	Vozovaia, M.A. (1977). [The effect of dichloroethane on the sexual cycle and embryogenesis of experimental animals]. Akusherstvo i Ginekologiya 2(2):57-59.
Health	Immune/Hematological; Hepatic/Liver; Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Mortality; Nutritional/Metabolic;
Outcome(s):	
Reported Health	Immune/Hematological: Leukoctye concentration and phagocytic activity; Hepatic/Liver: Functional tests, possibly liver weight; Reproduc-
Effect(s):	tive/Developmental: Estrous cycle parameters, pathology of reproductive organs, mating and fertility, and/or fetal development; Musculoskeletal: Functional tests for muscular activity (the summation-threshold index, the effect of angular acceleration, the Quick–Pytel test, the swim test, etc.); Neurological/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights;
<b>Duration:</b>	Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
HEDO ID.	(2)(2)

**HERO ID:** 62623

HERO ID: 62623			
Domain	Metric	Rating	Comments
Metric 17:	Consistency of Outcome Assessment	Low	Immune/Hematological: No detailed information regarding the execution of the study protocol for outcome assessment was provided. The timing of when immune effects were measured was only indicated as "every month," during the 4 month phase (and GDs 1 and 17) and it was mentioned that phagocytic activity was measured with to white staphylococcus culture. No other details were provided.; Hepatic/Liver: No detailed information regarding the execution of the study protocol for outcome assessment was provided. The timing of when animals were evaluated for liver effects was not reported.; Reproductive/Developmental: No detailed information regarding the execution of the study protocol for outcome assessment was provided. A time frame for the evaluation of some endpoints was indicated (e.g., every month) without specific details. The study indicated that animals were sacrificed on GDs 17-19 (wide range for the evaluation of some effects such as fetal body weights).; Musculoskeletal: No detailed information regarding the execution of the study protocol for outcome assessment was provided.; Neurological/Behavioral: No detailed information regarding the execution of the study protocol for outcome assessment was provided. The timing of when neurological tests (e.g., swim test) were measured was not specified in the study report.; Mortality: No detailed information regarding the execution of the study protocol for outcome assessment was provided. The timing of when animals were evaluated for mor tality (e.g., number of times daily) was not reported.; Nutritional/Metabolic: No detailed information regarding the execution of the study protocol for outcome assessment was provided. The timing of when body weights were measured was not specified in the study report.
Metric 18:	Sampling Adequacy	Low	All Outcomes: Details regarding sampling were not reported.
Metric 19:	Blinding of Assessors	N/A	Immune/Hematological: Blinding was not required by study type. The immune responses measured were not subjective.; Hepatic/Liver: Blinding was not required by study type.; Reproductive/Developmental: Blinding was not required by study type. Most of the outcomes evaluated were not subjective.; Musculoskeletal: Blinding was no required by study type.; Neurological/Behavioral: Blinding was not required by study type.; Mortality: Blinding was not required by study type. Mortality: Blinding was not required by study type. Body weights are not a subjective outcome.

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Study Citation:	Vozovaia, M.A. (1977). [The effect of dichloroethane on the sexual cycle and embryogenesis of experimental animals]. Akusherstvo i Ginekologiya 2(2):57-59.
Health	Immune/Hematological; Hepatic/Liver; Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Mortality; Nutritional/Metabolic;
Outcome(s):	
Reported Health	Immune/Hematological: Leukoctye concentration and phagocytic activity; Hepatic/Liver: Functional tests, possibly liver weight; Reproduc-
Effect(s):	tive/Developmental: Estrous cycle parameters, pathology of reproductive organs, mating and fertility, and/or fetal development; Musculoskeletal: Functional tests for muscular activity (the summation-threshold index, the effect of angular acceleration, the Quick–Pytel test, the swim test, etc.); Neurological/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights;
<b>Duration:</b>	Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
HERO ID:	62623

Domain		Metric	Rating	Comments
M	etric 20:	Negative Control Response	Low	Immune/Hematological: The biological response of the negative controls was not reported for immunological effects. Control responses were only reported for significant effects; immunological effects were reportedly not significant.; Hepatic/Liver: The biological response of the negative controls was not reported. Control responses were only reported for significant effects; no significant hepatotoxicity was reportedly observed.; Reproductive/Developmental: The biological response of the negative controls, when reported, appeared appropriate (estrous cycle parameters, preimplantation loss). However, control responses were only reported for significant effects. The rate of embryonic mortality on controls exceeded 10% (11%).; Musculoskeletal: The biological response of the negative controls was not reported. Control responses were only reported for significant effects; no significant effects on muscular activity were presumably observed.; Neurological/Behavioral: The biological response of the negative controls was not reported for neurological effects (behavior). Control responses were only reported for significant effects; neurological effects were reportedly not significant.; Mortality: The biological response of the negative controls was not reported for significant effects; no significant effects on mortality were reportedly observed.; Nutritional/Metabolic: The biological response of the negative controls was not reported for systemic effects (body weights). Control responses were only reported for significant effects; effects on body weight were reportedly not significant.
omain 6: Confounding / Va	ariable Co	ntrol		
	etric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Information on confounding factors (e.g., respiratory rate) were not reported.
M	etric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate (in either direction) that there were difference among groups in health outcomes unrelated to exposure.
М	etric 23:	Data Presentation and Analysis	Low	Immune/Hematological: Statistical analyses were performed but not described at all in the study report.; Hepatic/Liver: Statistical analyses were presumably performed but not described at all in the study report.; Reproductive/Developmental: Statistical analyses were performed but not described at all in the study report.; Musculoskeletal: Statistical analyses were presumably performed but not described at all in the study report.; Neurological/Behavioral: Statistical analyses were performed but not described at all in the study report.; Mortality: Statistical analyses were performed but not described at all in the study report. It is not entirely clear if statistical analyses were applied to mortality data.; Nutritional/Metabolic: Statistical analyses were performed but not described at all in the study report.

effects on mortality, incidence data were not shown.; Nutritional/Metabolic: Data presentation was inadequate. Numerical data were provided only for endpoints for which statistically significant effects were observed. Since there was no significant effect on body weights, the data for body weights were not shown (and it could not be determined

if body weights of treated animals remained within 10% of controls).

#### ... continued from previous page

**Study Citation:** Vozovaia, M.A. (1977). [The effect of dichloroethane on the sexual cycle and embryogenesis of experimental animals]. Akusherstvo i Ginekologiya 2(2):57-59.

Health Immune/He

Outcome(s):

Immune/Hematological; Hepatic/Liver; Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Mortality; Nutritional/Metabolic;

Reported Health Effect(s):

Immune/Hematological: Leukoctye concentration and phagocytic activity; Hepatic/Liver: Functional tests, possibly liver weight; Reproductive/Developmental: Estrous cycle parameters, pathology of reproductive organs, mating and fertility, and/or fetal development; Musculoskeletal: Functional tests for muscular activity (the summation-threshold index, the effect of angular acceleration, the Quick—Pytel test, the swim test, etc.); Neurologi-

cal/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights;

Duration: Chemical: Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane

Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane

**HERO ID:** 62623

Domain Metric Rating Comments Metric 24: Reporting of Data Uninformative Immune/Hematological: Data presentation was inadequate. Numerical data were provided only for endpoints for which statistically significant effects were observed. Since there was no significant immunological effects, data were not shown.; Hepatic/Liver: Data presentation was inadequate. Numerical data were provided only for endpoints for which statistically significant effects were observed. Since there were no effects liver effects reported, no data were shown.; Reproductive/Developmental: Data presentation was inadequate. Numerical data were provided only for endpoints for which statistically significant effects were observed.; Musculoskeletal: Data presentation was inadequate. Numerical data were provided only for endpoints for which statistically significant effects were observed. Since there were no effects on muscular activity reported, no data were shown.; Neurological/Behavioral: Data presentation was inadequate. Numerical data were provided only for endpoints for which statistically significant effects were observed. Since there was no significant neurological effects, data were not shown.; Mortality: Data presentation was inadequate. Numerical data were provided only for endpoints for which statistically significant effects were observed. Since there were no

**Overall Quality Determination** 

Uninformative

**Study Citation:** Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya

1:31-38. Neurological/Behavioral Health

**Outcome(s):** 

Clinical signs, conditioned reflex responses, morphological examinations of cerebral cortex Reported Health

Effect(s):

Chronic (>91 days) 6-months **Duration:** 

**Chemical:** 1,1-Dichloroethane- Isomer: dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	Low	The test substance was identified as dichloroethane. A CASRN was not reported leaving uncertainty about the isomer used.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity was not reported.
Domain 2: Test Design	gn			
	Metric 4:	Negative and Vehicle Controls	Uninformative	Negative control group was not included. The text reported "increased" or "decreased" changes is suggestive of a comparator (likely baseline measurements); however, this was not explicitly reported resulting in significant uncertainty.
	Metric 5:	Positive Controls	N/A	It is not clear that positive controls are required
	Metric 6:	Randomized Allocation of Animals	Low	Details of animal allocation into groups were not provided.
Domain 3: Exposure	Characterization			
Domain 3. Exposure	Metric 7:	Preparation and Storage of Test	Low	No details on the preparation of the test substance or storage conditions were reported.
	Metric 8:	Substance Consistency of Exposure Administration	Low	No details on the exposure administration were reporte.
	Metric 9:	Reporting of Doses/Concentrations	Low	What are presumed to be nominal concentrations were reported. There is no indication that atmospheres were analytically measured.
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were exposed 4 hrs/day for 6 months. No justification was provided for the exposure frequency and duration selected. This was a non-guideline study, and cannot be compared to other study types.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Two exposure concentrations were tested. No clear justifications for the selected concer trations was provided, but a dose-response was observed.
	Metric 12:	Exposure Route and Method	Uninformative	Animals were exposed via inhalation, but the type of exposure (e.g., whole body or nose only, or static or dynamic) was not specified. There were no descriptions of the inhalation chamber.
D : 4 T : 4 :	1			
Domain 4: Test Anin	nals Metric 13:	Test Animal Characteristics	Low	The study used white rats. No additional details of the test animals were provided.
	Metric 14:	Adequacy and Consistency of Animal	Low	No animal husbandry details were provided.
	Medic 14.	Husbandry Conditions	LOW	To allima hasoladiy details were provided.
	Metric 15:	Number of Animals per Group	Low	The number of animals included in the study was not reported.

HERO ID: 18135 Table: 1 of 1

## ... continued from previous page

**Study Citation:** Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya

Health Neurological/Behavioral

**Outcome(s):** 

Reported Health

Clinical signs, conditioned reflex responses, morphological examinations of cerebral cortex

Effect(s):

**Duration:** Chronic (>91 days) 6-months

Chemical: 1,1-Dichloroethane- Isomer: dichloroethane

**HERO ID:** 18135

Domain	Domain Metric		Rating	Comments
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	No methods or protocols for the outcomes assessed were provided.
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding execution of the methods for outcome assessment were not reported.
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling were not reported.
	Metric 19:	Blinding of Assessors	Low	The study did not report whether assessors were blinded to treatment group for subjective outcomes, and this deficiency is likely to have a substantial impact on results.
	Metric 20:	Negative Control Response	Low	No quantitative data were provided. It is unclear if the baseline measurements, which are assumed to be used as a comparator, were appropriate.
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Insufficient information was reported to determine confounding. It was not reported whether respiratory rates were monitored for a respiratory irritant.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Uninformative	There is no indication that statistical analysis was performed and no data enabling an independent statistical analysis were provided.
	Metric 24:	Reporting of Data	Uninformative	Results were not presented in a way allowing adequate interpretation of the results.

# **Overall Quality Determination**

## Uninformative

			•		
Human	Health	Hazard	Animal	Toxicology	Evaluation

<b>Study Citation:</b>	Brondeau, M.T., Bonnet, P., Guenier, J.P., De, C.J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters				
Health	19(1-2):139-146. Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)				
Outcome(s):	The patter Liver (Sertain enzyme activity for liver damage biolinarices, SDH, GEDH, GOT, and GLI.)				
Reported Health	Serum enzyi	me activities (units per ml (U/ml), or nmol pe	r min per ml) o	of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydroge-	
Effect(s):	nase (GLDF	I) and sorbitol dehydrogenase (SHD).	•		
<b>Duration:</b>	Acute (less t	than or equal to 24 hr) Acute- 4 hour			
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane			
HERO ID:	200247				
Domain		Metric	Rating	Comments	
Domain 1: Test Substance		T . G	*** 1		
	Metric 1:	Test Substance Identity	High	Test substance was identified in nomenclature as 1,2-dichloroethane; no CASRN.	
	Metric 2:	Test Substance Source	Low	The source of the test substance was Merck. Batch/lot numbers were not provided. Covers the lack of test substance identity in Metric 1 that did not report CASRN or chemical structure without double counting quality metrics.	
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported as >99.0%.	
Domain 2: Test Design					
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	Negative controls were exposed to clean filtered air.	
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.	
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report if/how animals were allocated.	
				1	
Domain 3: Exposure Ch					
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage are not adequately described given the volatility of the test substance.	
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure were limited; however, this is unlikely to substantially impact results. Unreported why the 6 chemicals tested in the study had different number of doses. Some chemicals tested at 4 doses, one tested at 5, some tested at 6.	
	Metric 9:	Reporting of Doses/Concentrations	Medium	Target concentrations were not reported. Chemical concentration levels are means of 3 samples or more with continuous monitoring, with a coefficient of variation of $< 13\%$ .	
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate. Single 4 hour exposure or 6 hour exposure (2 or 4 days).	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Single 4 hour: The number of dose groups was appropriate to elicit a full range or responses.	
	Metric 12:	Exposure Route and Method	Medium	Dynamic whole body inhalation chambers were used with adjustable air flows of air (10-12 m3/hr). Unknown distribution of test substance in the whole body inhalation chamber, since not reported, despite describing sampling methods. Uncertainty in parameters related to using the whole body inhalation chamber, like the number of air changes (minimum of 10/hr being required), and weather the cages were big enough for the rats and unknown how the rats were caged, possibly with more than one rat per cage.	
Domain 4: Test Animals	<b>,</b>				
	Metric 13:	Test Animal Characteristics	Medium	Age of rats and individual body weights at study initiation were not reported.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	No husbandry conditions were not reported, except that food and water were not available during exposure	
		Continu	ued on next pa	ege	
			ige 213 of 95	_	
1 450 210 01 700					

Study Citation:	Brondeau, M.T., Bonnet, P., Guenier, J.P., De, C.J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters					
•	19(1-2):139-146.					
Health	· · · · · · · · · · · · · · · · · · ·					
Outcome(s): Reported Health	Comm on zv	no activities (units per ml (II/ml), or amal per	or min nor ml) of	Fliver handstavicity higherters ALT (CDT) AST (COT) glutamete debydrage		
Effect(s):	Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SHD).					
Duration:		han or equal to 24 hr) Acute- 4 hour				
Chemical:						
HERO ID:	200247					
Domain		Metric	Rating	Comments		
	Metric 15:	Number of Animals per Group	Medium	The number of animals treated per group was appropriate (n=8)		
D : 5 O :						
Domain 5: Outcome	Assessment Metric 16:	Outcome Assessment Methodology	Low	Histology and organ weight were not assessed (only serum chemistry).		
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding outcome assessment were limited. This is especially uncertain given		
	weate 17.	Consistency of Gutcome Assessment	Low	the only measurements made were serum chemistry with no contextualization from body weights, liver weight, liver histology. The study authors did report that "The choice of seric parameters and sampling time was the result of preliminary experiments conducted to point out the best experimental conditions and not reported here." However, there was no reference or information provided on those parameters, which leaves uncertainty in outcome assessment consistency.		
	Metric 18:	Sampling Adequacy	High	Data are means +/- SE for 8 rats in each treatment group for the first, single 4-hour acute exposure. Seems sufficient since serum enzyme activity was the only outcome measure for liver-related biomarkers. Table 1.		
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study type.		
	Metric 20:	Negative Control Response	High	Negative control response was reported and appropriate. Used a manufacturer kit to measure serum enzyme activity for liver damage biomarkers. The authors stated, 'diagnostic kits purchased from Boehringer Mannheim,France," and "Quality controls were systematically performed (Precinorm E and S, Boehringer)."GOT and GPT appeared to have high background/values for negative control compared to test substance exposure (Table 1).		
Damain & Confound	ina / Variabla Car	ntual				
Domain 6: Confound	Metric 21:	Confounding Variables in Test Design	Low	Study did not report all information to determine confounding, reported information		
	Wether 21.	and Procedures	LOW	did not identify differences.1,2-dichloroethane is a respiratory irritant and toxicant, without respiration rate information nor other individual animal information, e.g., body weights, food and water consumption, a low confidence level is most appropriate.(EPA) https://www.epa.gov/sites/default/files/2016-09/documents/ethylene-dichloride.pdf(NJ DEH) https://nj.gov/health/eoh/rtkweb/documents/fs/0652.pdf		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.		
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed (Student's t-test).		
	Metric 24:	Reporting of Data	High	Exposure related to stated outcomes of interest were reported.		

HERO ID: 200279 Table: 1 of 1

**Study Citation:** Cottalasso, D., Domenicotti, C., Traverso, N., Pronzato, M., Nanni, G. (2002). Influence of chronic ethanol consumption on toxic effects of 1,2dichloroethane: glycolipoprotein retention and impairment of dolichol concentration in rat liver microsomes and Golgi apparatus. Toxicology 178(3):229-240. Hepatic/Liver Health Outcome(s):

Reported Health Clinical chemistry/enzyme activities, histopathology of liver (hepatic steatosis)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute (single exposure on one day)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metri	c 1: Test Substance Identity	High	The study authors reported using an appropriate concurrent negative control group.
Metri	c 2: Test Substance Source	Low	Manufacturer is reported; however, batch/lot number is not reported.
Metri	c 3: Test Substance Purity	High	Purity not reported, but test substance was analytical grade.
Domain 2: Test Design			
Metri	c 4: Negative and Vehicle Controls	High	The study authors reported using an appropriate concurrent negative control group.
Metr	c 5: Positive Controls	N/A	A positive control was not included in the study and is not required for this study type.
Metri	c 6: Randomized Allocation of Anima	als Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Character	zation		
Metri	c 7: Preparation and Storage of Test Substance	Low	Method of preparation of the test substance and storage (if not prepared immediately before treatment) were not reported and lack of details could impact results due to potential volatility of the test substance.
Metr	c 8: Consistency of Exposure	Low	Gavage dosing volume was not reported.
Metri	Administration Reporting of Doses/Concentration	ns High	Administered doses were reported without ambiguity.
Metri			The exposure frequency and duration of exposure were reported and both were appropriate for this study type and the outcomes of interest.
Metri	c 11: Number of Exposure Groups Dose/Concentration Spacing	s and Medium	There was only one dose group with 1,2-dichloroethane (DCE) exposure, which was adequate to induce liver effects, and the study purpose was to compare effects of DCE to teratment also with ethanol, not establish a dose response, so I scored this metric as medium.
Metri	c 12: Exposure Route and Method	High	The route and method of exposure were reported and were appropriate for the test substance.
Domain 4: Test Animals			
Metri	c 13: Test Animal Characteristics	Medium	Test animal age was not reported, but other characteristics (sex, strain, starting body weight, source) were reported, and the lack of information on test animal age is not expected to substantially impact the results, so scored this as medium.
Metri	c 14: Adequacy and Consistency of A Husbandry Conditions	animal High	All husbandry conditions were reported (including temperature, humidity, light-dark cycle, diet) and were adequate and the same for control and exposed groups.

**Study Citation:** Cottalasso, D., Domenicotti, C., Traverso, N., Pronzato, M., Nanni, G. (2002). Influence of chronic ethanol consumption on toxic effects of 1,2dichloroethane: glycolipoprotein retention and impairment of dolichol concentration in rat liver microsomes and Golgi apparatus. Toxicology 178(3):229-

240. Hepatic/Liver

Outcome(s):

Reported Health

Clinical chemistry/enzyme activities, histopathology of liver (hepatic steatosis)

Effect(s):

Health

**Duration:** Acute (less than or equal to 24 hr) Acute (single exposure on one day)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID: 200279

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (groups of 10 females) was reported, appropriate for the study type and outcome analysis, and consistent with studies of the same or similar type.
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest and the assessment methodology was sensitive and appropriate for the outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding execution of the protocol for collecting blood and liver samples were poorly detailed (e.g., timing for different groups following last dose is not stated for all measurements).
	Metric 18:	Sampling Adequacy	High	The information supplied indicates the use of adequate sampling for the outcomes of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for the endpoints/outcomes evaluated (e.g., clinical chemistry, initial histopathology review).
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described and sufficient data (e.g., means with standard deviations) were provided to conduct an independent statistical analysis.
	Metric 24:	Reporting of Data	Low	Data were reported adequately for only some outcomes, including serum enzymes (means with S.D.) and mechanistic data (e.g., MDA and dolichol concentrations). Data were not adequately reported for histopathology of liver (incidence not reported for treated vs. control groups; data only described in text).

# **Overall Quality Determination**

## Medium

<b>Study Citation:</b>	Cottalasso, D., Fontana, L., Gazzo, P., Dapino, D., Domenicotti, C., Pronzato, M.A., Nanni, G. (1995). Effects of 1,2-dichloroethane intoxication on
	dolichol levels and glycosyltransferase activities in rat liver microsomes and Golgi apparatus. Toxicology 104(1-3):63-71.

Health Hepatic/Liver

**Outcome(s):** 

**Reported Health** Liver weight, liver protein, serum AST, ALT, and TG, liver dolichol

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute oral in rats **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200280

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	Identified by name as 1,2-dichloroethane. CASRN was not provided.
	Metric 2:	Test Substance Source	Low	Test substance was obtained from a commercial source. The batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Purity and or grade was not reported.
Domain 2: Test Design	1			
6	Metric 4:	Negative and Vehicle Controls	Low	A negative control was included, but details regarding the control group were not reported (untreated vs. a vehicle control).
	Metric 5:	Positive Controls	N/A	A positive control is not necessary for this study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups
Domain 3: Exposure C	haracterization			
•	Metric 7:	Preparation and Storage of Test	Low	The test material was prepared as a solution 50% v/v in mineral oil.
	Metric 8:	Substance Consistency of Exposure Administration	Low	Details of administration were insufficiently reported, the gavage volume(s) used is unclear. It is unclear whether volumes were consistent across groups.
	Metric 9:	Reporting of Doses/Concentrations	Low	Doses are not clearly reported. The text indicates that animals were administered "single doses of DCE (ul/g body wt.) as a solution 50% v/v in mineral oil." It is unclear if the volume/bw administered was specific to the test substance, or referred to the 50% solution. A range of initial animal body weights was provided.
	Metric 10:	Exposure Frequency and Duration	High	Animals were administered a single dose, via gavage
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 5 groups, including controls.
	Metric 12:	Exposure Route and Method	High	The route of exposure (gavage) was considered acceptable.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Medium	Animal age was not reported, only male rats were used.
	Metric 14:	Adequacy and Consistency of Animal	High	Animal husbandry was adequately reported
	Metric 15:	Husbandry Conditions Number of Animals per Group	Low	There was some ambiguity in reporting. The methods report use of 4-6 animals/experimental group, but data tables report the data are means from 4-6 experiments. Was there 1 animal per group and the experiment was performed 4-6 times, or were there 4-6 animals/group and the experiment was performed once?
		Continu	und on novt no	

Reported information indicates the study used adequate sampling for the outcome(s) of

Blinding is not necessary for the outcomes evaluated

Negative control responses appeared to be appropriate.

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Study Citation:	Cottalasso, D., Fontana, L., Gazzo, P., Dapino, D., Domenicotti, C., Pronzato, M.A., Nanni, G. (1995). Effects of 1,2-dichloroethane intoxication on dolichol levels and glycosyltransferase activities in rat liver microsomes and Golgi apparatus. Toxicology 104(1-3):63-71. Hepatic/Liver							
Health								
Outcome(s):								
Reported Health	Liver weight	Liver weight, liver protein, serum AST, ALT, and TG, liver dolichol						
Effect(s):		•						
Duration:	Acute (less t	han or equal to 24 hr) Acute oral in rats						
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	200280	,						
Domain		Metric	Rating	Comments				
Domain 5: Outcome	Assessment							
	Metric 16:	Outcome Assessment Methodology	Medium	Outcome assessment methodology partially addressed the intended outcomes of interest Animals were sacrificed (at maximum) 60 minutes post-dosing. This timing is unlikely to be appropriate to detect changes in liver weights.				
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups				

High

N/A

High

Domain 6: Confoun	ding / Va	riable Control
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Metric 18:

Metric 19:

Metric 20:

Sampling Adequacy

Blinding of Assessors

Negative Control Response

ig / variable Coi	1001		
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups
Metric 22:	Health Outcomes Unrelated to	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure

(e.g., infection) that could influence the outcome assessment.

Metric 23: Data Presentation and Analysis High Statistical analysis were clearly described and were appropriate for the outcomes of interest.

Metric 24: Reporting of Data High Quantal data were clearly presented for all dose-groups as means +/- SD; statistical

results were included.

**Overall Quality Determination** 

Medium

# July 2024 Human Health Hazard Animal Toxicology Evaluation

Study Citation:		• • • • • • • • • • • • • • • • • • • •		F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J.A. (1999). Evaluation of 10 aliphatic
Health		hydrocarbons in the mouse bone marrow my (Genotoxicity)	ıcronucleus	test. Mutagenesis 14(2):207-215.
Outcome(s):		3,		
Reported Health	In vivo bone	marrow micronucleus test		
Effect(s):				
<b>Duration:</b>	Acute (less t	han or equal to 24 hr) single dose		
Chemical:		bethane- Isomer: 1,2-Dichloroethane		
HERO ID:	194679	,		
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Chemical name and CAS number identified.
	Metric 2:	Test Substance Source	High	Source identified; no batch or lot number was reported.
	Metric 3:	Test Substance Purity	High	Purity reported as 98.5%
Domain 2: Test Design				
2, 160, 260, 201	Metric 4:	Negative and Vehicle Controls	High	Vehicle control was used (olive oil)
	Metric 5:	Positive Controls	Medium	Colchicine and mitomycin C were tested as positive controls; a positive response was observed
	Metric 6:	Randomized Allocation of Animals	Medium	The study noted that mice were randomly allocated to treatment groups for the main in vivo bone marrow micronuleus test; it is not specified how the animals were randomized.
Domain 3: Exposure Ch	aracterization			
Domain 5. Exposure en	Metric 7:	Preparation and Storage of Test	Medium	Limited test substance preparation details were provided; noted olive oil was used as
		Substance		a vehicle at 10 ml/kg bd wt. It is a single dose study; therefore, omission of details are unlikely to have an impact on the study.
	Metric 8:	Consistency of Exposure Administration	High	Single i.p. dose exposure administered consistently
	Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity in the results section.
	Metric 10:	Exposure Frequency and Duration	High	Single dose
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The administered doses were reported in a range; dose levels were selected on the basis of published LD50 values.
	Metric 12:	Exposure Route and Method	High	i.p. exposure
Domain 4: Test Animals				
Domain 7. Test Amiliais	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and source was reported; no starting age was reported and only the
				terminal weights were reported
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry conditions were reported for the main in vivo bone marrow micronucleus test
	Metric 15:	Number of Animals per Group	Medium	5 animals/sex were tested for the bone marrow micronucleus assay
Domain 5: Outcome Ass	sessment			
I Succession I los	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was reported and scoring method described.
	Metric 10.	Outcome Assessment Methodology	111511	The outcome assessment methodology was reported and scoring method described.

		conun	uea from p	previous page				
Study Citation:	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J.A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. Mutagenesis 14(2):207-215.							
Health	Genotoxicity	(Genotoxicity)						
Outcome(s):								
Reported Health	In vivo bone	marrow micronucleus test						
Effect(s):								
Duration:	Acute (less t	han or equal to 24 hr) single dose						
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane						
HERO ID:	194679							
Domain		Metric	Rating	Comments				
	Metric 17:	Consistency of Outcome Assessment	High	Details of the assessment protocol were reported including harvest/scoring times				
	Metric 18:	Sampling Adequacy	High	5 animals/sex				
	Metric 19:	Blinding of Assessors	N/A	Not applicable				
	Metric 20:	Negative Control Response	High	The biological response of the control was appropriate and adequate; "the incidence of micronucleated PCEs in vehicle-treated mice was within the accepted spontaneous range for this strain of mouse with no significant sex differences"				
Domain 6: Confoundin	g / Variable Co	ntrol						
omani or comoundi.	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding factors; however, reported information did not identify differences among study groups				
	Metric 22:	Health Outcomes Unrelated to Exposure	High	There was no attrition in animals in any treated animal or controls				
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described; incidence were compared by X-square test, control- ling for within group heterogenieity with analysis of variance. PCE/NCE ration were compared by t-test.				
	Metric 24:	Reporting of Data	High	Data for exposure-related findings were presented for all outcomes by exposure group and sex				

### **Overall Quality Determination**

## High

HERO ID: 194679 Table: 2 of 3

**Study Citation:** Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J.A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. Mutagenesis 14(2):207-215. Health Clinical signs (Clinical signs of toxicity) Outcome(s): Reported Health Acute clinical signs of toxicity: piloerection, hypoactivity, hunched posture, sedation, shallow breathing Effect(s): **Duration:** Acute (less than or equal to 24 hr) single dose Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 194679 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Chemical name and CAS number identified. Metric 2: Test Substance Source High Source identified; no batch or lot number was reported. Metric 3: **Test Substance Purity** High Purity reported as 98.5% Domain 2: Test Design Metric 4: Negative and Vehicle Controls N/A It is not clear if negative controls were used for the preliminary acute toxicity test, though no control is required for acute lethality tests. Metric 5: Positive Controls N/A Not required for this study design Metric 6: Randomized Allocation of Animals Low The study noted that mice were randomly allocated to treatment groups for the main in vivo bone marrow micronuleus test; however, did not specify if this was done in the preliminary toxicity trials. The preliminary toxicity trials were noted to have followed the EEC guideline B.1 and OECD 401, which required that animals are randomly selected Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium Limited test substance preparation details were provided; noted olive oil was used as a vehicle at 10 ml/kg bd wt.; it is a single dose study; therefore, omission of details are Substance unlikely to have an impact on the study. Metric 8: Consistency of Exposure Low Details of exposure administration are incompletely reported for the acute lethality toxicity test Administration Reporting of Doses/Concentrations Metric 9: Low Administered doses were reported as a range **Exposure Frequency and Duration** Metric 10: High Single dose Metric 11: Number of Exposure Groups and Uninformative The administered doses were reported in a range; it is unclear how many doses were Dose/Concentration Spacing tested. dose levels were selected on the basis of published LD50 values. Metric 12: Exposure Route and Method High i.p. exposure Domain 4: Test Animals Metric 13: Test Animal Characteristics Medium Species, strain, sex, and source was reported; no starting age was reported and only the terminal weights were reported Metric 14: Adequacy and Consistency of Animal Animal husbandry conditions were reported for the main in vivo bone marrow micronu-Low cleus test; however, husbandry conditions for the preliminary toxicity test were not; it is **Husbandry Conditions** unclear if they were similar. Metric 15: Number of Animals per Group Low 5 animals/sex were tested for the preliminary toxicity test; number of animals were not reported in the methods section but were reported in the results table. It is unclear how many dose groups there were and it is unclear if 5 animals per dose group were tested

HERO ID: 194679 Table: 2 of 3

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Study Citation: Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J.A. (1999). Evaluation of 10 aliphatic

halogenated hydrocarbons in the mouse bone marrow micronucleus test. Mutagenesis 14(2):207-215.

**Health** Clinical signs (Clinical signs of toxicity)

**Outcome(s):** 

Reported Health

Acute clinical signs of toxicity: piloerection, hypoactivity, hunched posture, sedation, shallow breathing

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194679

Domain		Metric	Rating	Comments
Domain 5: Outcome Assessme	ent			
Met	ric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology was partially addressed; observations of clinical signs of toxicity
Meta	ric 17:	Consistency of Outcome Assessment	Low	There was incomplete reporting of details of outcome assessment protocol execution
Meta	ric 18:	Sampling Adequacy	Medium	5 animals/sex for a preliminary toxicity test; unclear if 5 animals per sex per dose
Meta	ric 19:	Blinding of Assessors	N/A	Not applicable
Meta	ric 20:	Negative Control Response	N/A	A negative control was not required
Domain 6: Confounding / Vari				
Met	ric 21:	Confounding Variables in Test Design and Procedures	Medium	The preliminary toxicity study did not report information to determine confounding variable, but no information was reported that identified differences among the group
Met	ric 22:	Health Outcomes Unrelated to Exposure	Medium	For the preliminary toxicity test, there was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure
Met	ric 23:	Data Presentation and Analysis	N/A	statistical analysis not necessary; observations of an acute toxicity test; incidence not reported.
Meta	ric 24:	Reporting of Data	Low	Clinical signs of toxicity were not reported by sex; incidence data were not reported

## **Overall Quality Determination**

## Uninformative

HERO ID: 194679 Table: 3 of 3

Study Citation: Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J.A. (1999). Evaluation of 10 aliphatic

halogenated hydrocarbons in the mouse bone marrow micronucleus test. Mutagenesis 14(2):207-215.

**Health** Mortality

**Outcome(s):** 

Reported Health

LD50

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194679

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	Chemical name and CAS number identified. 1,2-dichloroethane; CASRN 107-06-2
	Metric 2:	Test Substance Source	High	Source identified as C. Erba; no batch or lot number was reported.
	Metric 3:	Test Substance Purity	High	Purity reported as 98.5%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	It is not clear if negative controls were used for the preliminary acute toxicity test, though no control is required for acute lethality tests.
	Metric 5:	Positive Controls	N/A	not required for this study design
	Metric 6:	Randomized Allocation of Animals	Low	The study noted that mice were randomly allocated to treatment groups for the main in vivo bone marrow micronuleus test; however, did not specify if this was done in the preliminary toxicity trials. The preliminary toxicity trials were noted to have followed the EEC guideline B.1 and OECD 401, which required that animals are randomly selected
Domain 3: Exposure Ch	aracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Medium	Limited test substance preparation details were provided; noted olive oil was used as a vehicle at 10 ml/kg bd wt.; it is a single dose study; therefore, omission of details are unlikely to have an impact on the study.
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are incompletely reported for the acute lethality toxicity test
	Metric 9:	Reporting of Doses/Concentrations	Medium	Administered doses were reported as a range
	Metric 10:	Exposure Frequency and Duration	High	Single dose
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The administered doses were reported in a range; it is unclear how many doses were tested. dose levels were selected on the basis of published LD50 values. The LD50 was higher than the the upper range of administered doses
	Metric 12:	Exposure Route and Method	High	i.p. exposure
Domain 4: Test Animals				
Domain 4. Test Allilliais	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and source was reported; no starting age was reported and only the terminal weights were reported
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were reported for the main in vivo bone marrow micronucleus test; however, husbandry conditions for the preliminary toxicity test were not; it is unclear if they were similar.
	Metric 15:	Number of Animals per Group	Low	5 animals/sex were tested for the preliminary toxicity test; number of animals were not reported in the methods section but were reported in the results table. It is unclear how many dose groups there were and it is unclear if 5 animals per dose group were tested

## Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J.A. (1999). Evaluation of 10 aliphatic

halogenated hydrocarbons in the mouse bone marrow micronucleus test. Mutagenesis 14(2):207-215.

Health

Mortality

**Outcome(s):** 

Reported Health I

LD50

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194679

Domain		Metric	Rating	Comments
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology was partially addressed; observations of death and 24- and 48-hour LD50 are an appropriate outcome for this endpoint.
	Metric 17:	Consistency of Outcome Assessment	Medium	There was incomplete reporting of details of outcome assessment protocol execution, but unlikely to have substantial impact on results.
	Metric 18:	Sampling Adequacy	High	5 animals/sex for a preliminary toxicity test
	Metric 19:	Blinding of Assessors	N/A	Not applicable
	Metric 20:	Negative Control Response	N/A	A negative control was not required
Domain 6: Confoun	nding / Variable Con Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The preliminary toxicity study did not report information to determine confounding variable, but no information was reported that identified differences among the group
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	For the preliminary toxicity test, there was no information either to support or dismis the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure
	Metric 23:	Data Presentation and Analysis	Low	Methods used to derive LD50s were not reported.
	Metric 24:	Reporting of Data	Low	LD50 was not reported by sex; no confidence intervals were reported with the LD50; mortality incidence data were not reported

## **Overall Quality Determination**

Low

HERO ID: 10699112 Table: 1 of 4

**Study Citation:** Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.

Health Mortality; Clinical signs, gross necropsy (Clinical signs, gross necropsy);

**Outcome(s):** 

**Reported Health** Mortality: Mortality; Clinical signs, gross necropsy (Clinical signs, gross necropsy): Clinical signs (observations for abnormalities of the eye, reproductive Effect(s):

system, and skin or hair coat/mucous membranes, injury, missing extremities, palpable masses or swelling); gross necropsy of reproductive organs and

other unspecified organs/tissues (no effects observed).;

Acute (less than or equal to 24 hr) 4 hours **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 10699112

Domain		Metric	Rating	Comments
Domain 1: Test Substar	ice			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively: name, synonyms, molecular formula and weight were provided.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance manufacturer and lot number were provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance purity was 99%, and was verified using FTIR and GC/MS.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: This was an acute toxicity study, which would be used to "determine the exposure levels and the time of peak effect for subsequent inhalation and neurotoxicity testing."
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were neither used nor required.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study.
Domain 3: Exposure C	naracterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The test substance preparation was adequately described, and storage was not needed as it was a single 4 hour exposure.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposure conditions were continuously monitored to maintain temperature and relative humidity in the chamber. Chamber airflow data was collected to ensure chamber was kept at a negative pressure compared to the surrounding area.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: The nominal and analytical concentrations were provided, along with the measured chamber concentrations for every 30 minutes during the exposure.
	Metric 10:	Exposure Frequency and Duration	High	Mortality: The exposure information was completely reported (a single 4 hour exposure) and appropriate for an acute inhalations study.; Clinical signs, gross necropsy (Clinical signs, gross necropsy): The exposure information was completely reported (a single 4 hour exposure) and was appropriate for an acute inhalation study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The only dose was chosen based on the LC50 from a previous study and will be used to design future studies. Effects were seen at this dose, which may be transferable to future studies.
	Metric 12:	Exposure Route and Method	High	All Outcomes: A whole-body exposure chamber was used, with 12-15 air changes per hour.

#### Domain 4: Test Animals

		contin	ued from p	previous page		
Study Citation: Health Outcome(s):		cal, (2005). Ethylene dichloride: Acute vapolinical signs, gross necropsy (Clinical signs				
Reported Health Effect(s):	Mortality: Mortality; Clinical signs, gross necropsy (Clinical signs, gross necropsy): Clinical signs (observations for abnormalities of the eye, reproductive system, and skin or hair coat/mucous membranes, injury, missing extremities, palpable masses or swelling); gross necropsy of reproductive organs and other unspecified organs/tissues (no effects observed):					
Duration: Chemical: HERO ID:	other unspecified organs/tissues (no effects observed).; Acute (less than or equal to 24 hr) 4 hours 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 10699112					
Domain		Metric	Rating	Comments		
	Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, age, sex, and starting body weights were provided. The F-344 rat is a common model animal for inhalation exposure studies.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All animal husbandry conditions were reported (temperature, humidity, light/dark cycle, number of animals per cage, food and water administration).		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: This was an acute lethality study, so 5 rats/sex was appropriate.		
Domain 5: Outcome	Assessment					
	Metric 16:	Outcome Assessment Methodology	High	Mortality: The outcome assessment (mortality) addressed the purpose of the study.; Clinical signs, gross necropsy (Clinical signs, gross necropsy): The outcome assessment (clinical signs, gross necropsy) addressed the purpose of the study, acute toxicity.		
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: A cage-side examination was conducted at least once a day, preferably at the same time each day (usually in the morning).		
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for the study.		
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Only a single test group was used (no control) so blinding was not needed.		
	Metric 20:	Negative Control Response	N/A	All Outcomes: No control required		
Domain 6: Confound	ling / Variable Co	ntrol				
Domain of Companie	Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: Only a single test group, and no information to suggest confounders were present.		
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Mortality: Animals were examined by a veterinarian to determine their health status and daily observations were performed to catch any illness or injury.; Clinical signs, gross necropsy (Clinical signs, gross necropsy): Only a single test group, and only general clinical signs and a lack of gross necropsy findings were reported.		
	Metric 23:	Data Presentation and Analysis	High	Mortality: Lack of mortality provided qualitatively and statistical analysis was not needed.; Clinical signs, gross necropsy (Clinical signs, gross necropsy): Lack of gross necropsy findings provided qualitatively, and general clinical signs were provided for each animal (statistical analysis was not needed).		
	Metric 24:	Reporting of Data	High	Mortality: Lack of mortality provided qualitatively.; Clinical signs, gross necropsy (Clinical signs, gross necropsy): Lack of gross necropsy findings provided qualitatively, and general clinical signs were provided for each animal		
Overall Qua	lity Detern	nination	High			
	•					

HERO ID: 10699112 Table: 2 of 4

**Study Citation:** 

Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) 4 hours 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

**HERO ID:** 10699112

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively: name, synonyms, molecular formula and weight were provided.
	Metric 2:	Test Substance Source	High	The test substance manufacturer and lot number were provided.
	Metric 3:	Test Substance Purity	High	The test substance purity was 99%, and was verified using FTIR and GC/MS.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	This was an acute toxicity study, which would be used to "determine the exposure levels and the time of peak effect for subsequent inhalation and neurotoxicity testing."
	Metric 5:	Positive Controls	N/A	Positive controls were neither used nor required.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study.
Domain 3: Exposure Cl	haracterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	The test substance preparation was adequately described, and storage was not needed as it was a single 4 hour exposure.
	Metric 8:	Consistency of Exposure Administration	High	Exposure conditions were continuously monitored to maintain temperature and relative humidity in the chamber. Chamber airflow data was collected to ensure chamber was kept at a negative pressure compared to the surrounding area.
	Metric 9:	Reporting of Doses/Concentrations	High	The nominal and analytical concentrations were provided, along with the measured chamber concentrations for every 30 minutes during the exposure.
	Metric 10:	Exposure Frequency and Duration	High	The exposure information was completely reported (a single 4 hour exposure) and was adequate for an acute inhalation study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The only dose was chosen based on the LC50 from a previous study and will be used to design future studies. Effects were seen at this dose, which may be transferable to future studies.
	Metric 12:	Exposure Route and Method	High	A whole-body exposure chamber was used, with 12-15 air changes per hour.
Domain 4: Test Animal	ls			
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, age, sex, and starting body weights were provided. The F-344 rat is a common model animal for inhalation exposure studies.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All animal husbandry conditions were reported (temperature, humidity, light/dark cycle number of animals per cage, food and water administration).
	Metric 15:	Number of Animals per Group	Medium	This was an acute lethality study, so 5 rats/sex was appropriate.

Domain 5: Outcome Assessment

### Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

**Study Citation:** 

Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 4 hours **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 10699112

Domain		Metric	Rating	Comments
M	letric 16:	Outcome Assessment Methodology	High	The outcome measurement (body weight) addressed the overall assessment, acute toxic-
				ity.
M	letric 17:	Consistency of Outcome Assessment	High	Animals were weighed and examined prior to exposure to the test material and observed at least every 30 minutes during the exposure period. All surviving rats were weighed on test days 2, 4, 8, 11, and 15 during the two-week post-exposure period.
M	Ietric 18:	Sampling Adequacy	High	Sampling was adequate for the study.
M	letric 19:	Blinding of Assessors	N/A	Only a single test group was used (no control) so blinding was not needed.
M	letric 20:	Negative Control Response	N/A	No control required
Domain 6: Confounding / V	ariable Con	trol		
M	Ietric 21:	Confounding Variables in Test Design and Procedures	Medium	Slight body weight changes were measured, although food intake and water consumption was not.
M	letric 22:	Health Outcomes Unrelated to Exposure	High	Only a single test group, and no mortality was observed.
M	Metric 23:	Data Presentation and Analysis	High	Individual body weight data were provided, and statistical analysis was conducted on the mean.
M	letric 24:	Reporting of Data	High	Individual body weight data were provided along with sex means.

## **Overall Quality Determination**

## High

HERO ID: 10699112 Table: 3 of 4

**Study Citation:** Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats. Health Neurological/Behavioral Outcome(s): **Reported Health** Observations of response to touch, gait evaluation, behavior/movements (e.g., decreased activity, incoordination), palpebral closure, pupil size, lacrimation, Effect(s): reaction to stimuli, abnormal muscle movements, respiration, or posture, and resistance to removal from cage. **Duration:** Acute (less than or equal to 24 hr) 4 hours Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 10699112 Domain Metric Comments Rating Domain 1: Test Substance Metric 1: Test Substance Identity High The test substance was identified definitively: name, synonyms, molecular formula and weight were provided. Metric 2: Test Substance Source High The test substance manufacturer and lot number were provided. Metric 3: Test Substance Purity High The test substance purity was 99%, and was verified using FTIR and GC/MS. Domain 2: Test Design Metric 4: Negative and Vehicle Controls N/A This was an acute toxicity study, which would be used to "determine the exposure levels and the time of peak effect for subsequent inhalation and neurotoxicity testing." Metric 5: Positive Controls N/A Positive controls were neither used nor required. Metric 6: Randomized Allocation of Animals Medium Animals were stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test High The test substance preparation was adequately described, and storage was not needed as it was a single 4 hour exposure. Substance Metric 8: Consistency of Exposure High Exposure conditions were continuously monitored to maintain temperature and relative humidity in the chamber. Chamber airflow data was collected to ensure chamber was Administration kept at a negative pressure compared to the surrounding area. Metric 9: Reporting of Doses/Concentrations High The nominal and analytical concentrations were provided, along with the measured chamber concentrations for every 30 minutes during the exposure. Metric 10: Exposure Frequency and Duration High The exposure information was completely reported (a single 4 hour exposure). Number of Exposure Groups and The only dose was chosen based on the LC50 from a previous study and will be used to Metric 11: Medium design future studies. Effects were seen at this dose, which may be transferable to future Dose/Concentration Spacing studies. Metric 12: Exposure Route and Method High A whole-body exposure chamber was used, with 12-15 air changes per hour. Domain 4: Test Animals Metric 13: Test Animal Characteristics High The test animal species, strain, age, sex, and starting body weights were provided. The F-344 rat is a common model animal for inhalation exposure studies. Metric 14: Adequacy and Consistency of Animal High All animal husbandry conditions were reported (temperature, humidity, light/dark cycle, number of animals per cage, food and water administration). **Husbandry Conditions** Number of Animals per Group Medium Metric 15: This was an acute lethality study, so 5 rats/sex was appropriate. Domain 5: Outcome Assessment

Study Citation: Health Outcome(s):	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.  Neurological/Behavioral  Observations of response to touch, gait evaluation, behavior/movements (e.g., decreased activity, incoordination), palpebral closure, pupil size, lacrimation, reaction to stimuli, abnormal muscle movements, respiration, or posture, and resistance to removal from cage.  Acute (less than or equal to 24 hr) 4 hours  1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
Reported Health Effect(s): Duration: Chemical:							
HERO ID:	10699112						
Domain		Metric	Rating	Comments			
	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment methodologies (clinical observations for neurological/behavioral changes) were adequately described. Clinical observations are generally not a sensitive measure for neurological/behavioral effects, but the outcome assessment methodology is consistent with those included in an acute lethality study.			
	Metric 17:	Consistency of Outcome Assessment	High	A cage-side examination was conducted at least once a day, preferably at the same time each day (usually in the morning).			
	Metric 18:	Sampling Adequacy	High	Sampling was adequate for the study.			
	Metric 19:	Blinding of Assessors	N/A	Only a single test group was used (no control) so blinding was not needed.			
	Metric 20:	Negative Control Response	N/A	No control required			
Domain 6: Confoundir	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design	High	Only a single test group, and no information to suggest confounders were present.			
	Metric 22:	and Procedures Health Outcomes Unrelated to	High	Only a single test group, and no mortality was observed.			
	Metric 23:	Exposure Data Presentation and Analysis	N/A	The study included a single group without a control, statistical analysis was not needed			
	Metric 24:	Reporting of Data	High	Incidences of clinical observations were reported quantitatively.			

HERO ID: 10699112 Table: 4 of 4

**Study Citation:** 

Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.

Health

Gastrointestinal

**Outcome(s):** 

**Reported Health** Observations for abnormal urine or feces, abnormalities of the GI tract, excessive soiling

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 4 hours Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 10699112

11110 121	100//112			
Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively: name, synonyms, molecular formula and weight were provided.
	Metric 2:	Test Substance Source	High	The test substance manufacturer and lot number were provided.
	Metric 3:	Test Substance Purity	High	The test substance purity was 99%, and was verified using FTIR and GC/MS.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	N/A	This was an acute toxicity study, which would be used to "determine the exposure levels and the time of peak effect for subsequent inhalation and neurotoxicity testing."
	Metric 5:	Positive Controls	N/A	Positive controls were neither used nor required.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study.
Domain 3: Exposure C	haracterization			
Domain 3. Exposure C.	Metric 7:	Preparation and Storage of Test Substance	High	The test substance preparation was adequately described, and storage was not needed as it was a single 4 hour exposure.
	Metric 8:	Consistency of Exposure Administration	High	Exposure conditions were continuously monitored to maintain temperature and relative humidity in the chamber. Chamber airflow data was collected to ensure chamber was kept at a negative pressure compared to the surrounding area.
	Metric 9:	Reporting of Doses/Concentrations	High	The nominal and analytical concentrations were provided, along with the measured chamber concentrations for every 30 minutes during the exposure.
	Metric 10:	Exposure Frequency and Duration	High	The exposure information was completely reported (a single 4 hour exposure).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The only dose was chosen based on the LC50 from a previous study and will be used to design future studies. Effects were seen at this dose, which may be transferable to future studies.
	Metric 12:	Exposure Route and Method	High	A whole-body exposure chamber was used, with 12-15 air changes per hour.
Domain 4: Test Animal	ls			
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, age, sex, and starting body weights were provided. The F-344 rat is a common model animal for inhalation exposure studies.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All animal husbandry conditions were reported (temperature, humidity, light/dark cycle number of animals per cage, food and water administration).
	Metric 15:	Number of Animals per Group	Medium	This was an acute lethality study, so 5 rats/sex was appropriate.

#### Domain 5: Outcome Assessment

Study Citations	Daw Charai	and (2005) Ethyrlana diablasida. At		s toxicity aturby in Eigebon 244 note			
Study Citation: Health	Gastrointesti	cal, (2005). Ethylene dichloride: Acute vape	or innatation	toxicity study in Fischer 344 rats.			
Outcome(s):	Gastronicistinai						
Reported Health	Observations for abnormal urine or feces, abnormalities of the GI tract, excessive soiling						
Effect(s):							
Duration:	Acute (less than or equal to 24 hr) 4 hours						
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	10699112						
Domain		Metric	Rating	Comments			
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodologies (clinical observations for gastrointestinal effects and system-related gross necropsy) were adequately described. The outcome assessment methods were partially sensitive to the outcome of interest (histopathology was not conducted, but the methods were consistent with those included in an acute lethality study.			
	Metric 17:	Consistency of Outcome Assessment	High	A cage-side examination was conducted at least once a day, preferably at the same time each day (usually in the morning).			
	Metric 18:	Sampling Adequacy	High	Sampling was adequate for the study.			
	Metric 19:	Blinding of Assessors	N/A	Only a single test group was used (no control) so blinding was not needed.			
	Metric 20:	Negative Control Response	N/A	No control required			
Domain 6: Confoundin	or / Variable Co	ntrol					
Domain o. Comoundin	Metric 21:	Confounding Variables in Test Design and Procedures	High	Only a single test group, and no information to suggest confounders were present.			
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Only a single test group, and no mortality was observed.			
	Metric 23:	Data Presentation and Analysis	N/A	The study included a single group without a control, statistical analysis was not needed			
	Metric 24:	Reporting of Data	High	Incidences of clinical observations were reported quantitatively. The lack of gross effects was qualitatively reported.			
Overall Quali	ty Detern	nination	High				

HERO ID: 10699356 Table: 1 of 2

**Study Citation:** 

Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats.

Health

Mortality; Nutritional/Metabolic;

**Outcome(s):** 

**Reported Health** Mortality: Mortality (LC50); Nutritional/Metabolic: Body weight;

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 4 hours **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 10699356

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance (1,2-dichloroethane) was identified definitively (name, CAS no. , molecular weight, chemical formula and structure)
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was not explicitly reported, but the certificate of analysis citation (Bailey-Wyche 2016) references Fisher Scientific and the lot number. Purity was determined by GCMS (100%).
	Metric 3:	Test Substance Purity	High	All Outcomes: Substance purity was 100%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: This is an acute lethality/toxicity study which doe not require a negative control.
	Metric 5:	Positive Controls	N/A	All Outcomes: This is an acute lethality/toxicity study which doe not require a positive control.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study, although only a single dose group was tested.
Domain 3: Exposure Ch	paracterization			
Domain 3. Exposure Ci	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The test substance preparation and storage were described, however stability was not an issue as the test atmosphere was generated and immediately delivered to the system.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Details of the exposure administration were mostly reported, however it is not clear how many animals were exposed at a time, so it is unknown whether there was consistency in dosing the animals.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: The nominal and analytical concentrations were reported, along with an explanation as to why they varied. Chamber concentrations were measured twice an hour.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure concentration and duration were reported and appropriate for this type of study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	All Outcomes: This is an acute lethality study, which does not require dose-response information, and only a single concentration was used.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route and method of exposure were reported and appropriate for this study type.

#### Domain 4: Test Animals

Study Citation:	Dow Chemic	cal, (2017). [Redacted] 1,2-Dichloroethane:	Acute vapo	or inhalation toxicity study in F344/DuCrl rats.		
Health	Mortality; Nutritional/Metabolic;					
Outcome(s): Reported Health Effect(s):	Mortality: Mortality (LC50); Nutritional/Metabolic: Body weight;					
Duration:	Acute (less t	han or equal to 24 hr) 4 hours				
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	10699356					
Domain		Metric	Rating	Comments		
	Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, and age were reported in the methods, and the test animal was obtained from a commercial source. Starting body weights were found in the appendix along with study duration weights. The test species/strain was an appropriate model.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, water availability). Animals were housed in individual cages after assignment to the treatment groups and for exposure.		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: This study examine acute toxicity, so 5 animals/sex was sufficient.		
Domain 5: Outcome A	ssassmant					
Domain 3. Outcome A	Metric 16:	Outcome Assessment Methodology	High	Mortality: The outcome assessment addressed the intended outcome (mortality) and the assessment methodology was sensitive.; Nutritional/Metabolic: The outcome assessment addressed the intended outcome (body weight) and the assessment methodology was sensitive.		
	Metric 17:	Consistency of Outcome Assessment	High	Mortality: Details of the outcome assessment were reported (cage-side examination was conducted at least twice a day, generally at the same time each day).; Nutritional/Metabolic: Details of the outcome assessment were reported (Animals were weighed and examined prior to exposure to the test material and observed at least every 30 minutes during the exposure period. All surviving rats were weighed on test days 2, 4, 8, 11, 14 and 15 during the two-week post-exposure period).		
	Metric 18:	Sampling Adequacy	High	All Outcomes: There are no concerns with the sampling adequacy.		
	Metric 19:	Blinding of Assessors	N/A	Mortality: There was only a single exposure group, so blinding was not needed.; Nutritional/Metabolic: There was only a single exposure group, and body weight is not a subjective measure, so blinding was not needed.		
	Metric 20:	Negative Control Response	N/A	All Outcomes: This was an acute lethality study, so a negative control was not required.		
D : ( C C : 1'	/W : 11 G					
Domain 6: Confoundin	g / Variable Coi Metric 21:	Confounding Variables in Test Design	Medium	Mortality: Not enough information was provided to determine if confounders were		
	wicule 21.	and Procedures	Wicdiuiii	present (breathing parameters, food/water intake).; Nutritional/Metabolic: Not enough information was provided to determine if confounders may have been present (breathing parameters, food/water intake).		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that unrelated heath outcomes could have affected the data.		
	Metric 23:	Data Presentation and Analysis	N/A	Mortality: Statistical analysis was not required because only a single exposure group was tested.; Nutritional/Metabolic: Statistical analysis was conducted on the body weight data.		
	Metric 24:	Reporting of Data	High	Mortality: Mortality data were presented overall.; Nutritional/Metabolic: Body weight data were presented overall and for individual animals.		

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

HERO ID: 10699356 Table: 1 of 2

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**Study Citation:** Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats.

Health Mortality; Nutritional/Metabolic;

**Outcome(s):** 

**Reported Health** Mortality: Mortality (LC50); Nutritional/Metabolic: Body weight;

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 4 hours Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 10699356

Metric Domain Rating Comments

**Overall Quality Determination** High

HERO ID: 10699356 Table: 2 of 2

Study Citation: Health						
Outcome(s): Reported Health Effect(s):	Clinical signs (decreased/absent activity, decreased/absent reactivity to stimuli/decreased responsiveness to touch, decreased/increased resistance to removal, decreased extensor-thrust response, decreased muscle tone, soft/absent feces, circling, head bobbing, eyelids partially closed, inability to walk, poor coordination, increased lacrimation, cold to touch, thin, arched back, splayed hindlimbs, rapid respiration, ungroomed fur, soiling), gross necropsy					
Duration: Chemical: HERO ID:	coordination, increased lacrimation, cold to touch, thin, arched back, splayed hindlimbs, rapid respiration, ungroomed fur, soiling), gross necropsy Acute (less than or equal to 24 hr) 4 hours 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 10699356					
Domain		Metric	Rating	Comments		
Domain 1: Test Substan	ice					
	Metric 1:	Test Substance Identity	High	The test substance (1,2-dichloroethane) was identified definitively (name, CAS no. , molecular weight, chemical formula and structure)		
	Metric 2:	Test Substance Source	High	The test substance source was not explicitly reported, but the certificate of analysis citation (Bailey-Wyche 2016) references Fisher Scientific and the lot number. Purity was determined by GCMS (100%).		
	Metric 3:	Test Substance Purity	High	Substance purity was 100%		
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	N/A	This is an acute lethality/toxicity study which doe not require a negative control.		
	Metric 5:	Positive Controls	N/A	This is an acute lethality/toxicity study which doe not require a positive control.		
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study, although only a single dose group was tested.		
Domain 3: Exposure Ch	naracterization					
	Metric 7:	Preparation and Storage of Test Substance	High	The test substance preparation and storage were described, however stability was not an issue as the test atmosphere was generated and immediately delivered to the system.		
	Metric 8:	Consistency of Exposure Administration	Medium	Details of the exposure administration were mostly reported, however it is not clear how many animals were exposed at a time, so it is unknown whether there was consistency in dosing the animals.		
	Metric 9:	Reporting of Doses/Concentrations	High	The nominal and analytical concentrations were reported, along with an explanation as to why they varied. Chamber concentrations were measured twice an hour.		
	Metric 10:	Exposure Frequency and Duration	High	The exposure concentration and duration were reported and appropriate for this type of study.		
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	This is an acute lethality study, which does not require dose-response information, and only a single concentration was used.		
	Metric 12:	Exposure Route and Method	High	The exposure route and method of exposure were reported and appropriate for this study type.		
Domain 4: Test Animals						
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, and age were reported in the methods, and the test animal was obtained from a commercial source. Starting body weights were found in the appendix along with study duration weights. The test species/strain was an appropriate model.		
		Contin	nued on nex	at page		

Study Citation:	Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats. Clinical signs, gross necropsy (Clinical signs, gross necropsy)						
Health Outcome(s):	Clinical signs, gross necropsy (Clinical signs, gross necropsy)						
Reported Health	Clinical sign	s (decreased/absent activity decreased/abs	ent reactivit	y to stimuli/decreased responsiveness to touch, decreased/increased resistance to re-			
Effect(s):				oft/absent feces, circling, head bobbing, eyelids partially closed, inability to walk, poor			
Effect(s).				, splayed hindlimbs, rapid respiration, ungroomed fur, soiling), gross necropsy			
Duration:		han or equal to 24 hr) 4 hours	arched back	, sprayed mildimios, rapid respiration, ungroomed fur, soming), gross necropsy			
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	10699356						
Domain		Metric	Rating	Comments			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, water availability). Animals were housed in individual cages after assignment to the treatment groups and for exposure.			
	Metric 15:	Number of Animals per Group	Medium	This study examined acute toxicity, so 5 animals/sex was sufficient.			
Domain 5: Outcome A	Assessment Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment addressed the intended outcome (clinical signs, gross necropsy), although other outcomes may have been more sensitive (FOB, histopathology).			
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment were reported (cage-side examination was conducted at least twice a day, generally at the same time each day. A complete necropsy was conducted on all animals by a veterinary pathologist or by a trained technologist qualified to recognize common lesions.).			
	Metric 18:	Sampling Adequacy	High	There are no concerns with the sampling adequacy.			
	Metric 19:	Blinding of Assessors	N/A	There was only a single exposure group, so blinding was not needed.			
	Metric 20:	Negative Control Response	N/A	This was an acute lethality study, so a negative control was not required.			
Domain 6: Confounding	ng / Variable Cor	ntrol					
2 cmain of Comoditati	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Not enough information was provided to determine if confounders were present (breathing parameters, food/water intake).			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that unrelated heath outcomes could have affected the data.			
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not required because only a single exposure group was tested.			
	Metric 24:	Reporting of Data	High	Clinical signs and necropsy results were presented qualitatively overall and for individual animals.			
Overall Oual	Overall Quality Determination						

Human Health Hazard Animal Toxicology Evaluation HERO ID: 2799602 Table: 1 of 2

**Study Citation:** Dow Chemical, (1989). Comparison of the acute lethality of selected hydrocarbons via intratracheal and oral routes (final report) with attachments, cover

sheets and letter dated 061989. Mortality

Health **Outcome(s):** 

**Reported Health** 

Effect(s):

Mortality

**Duration:** 

Acute (less than or equal to 24 hr) Single intratracheal injection

**Chemical:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 2799602

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified as ethylene dichloride. The CASRN (107-06-2) was provided.
	Metric 2:	Test Substance Source	Low	A commercial source was named, but a lot and/or batch number was not provided.
	Metric 3:	Test Substance Purity	High	Reported as ACS (American Chemical Society) grade. The company website claims this is $99\%~\text{pure}.$
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	High	The study included surgical controls that were injected with saline. It is unclear that saline was used as a vehicle. The control animals were injected with 1 or 2 times the maximal volume of the test sustance.
	Metric 5:	Positive Controls	N/A	A positive control is not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on preparation was limited; it isn't specifically indicated whether a vehicle was used. Information on storage was not reported, but this is unlikely to have a substantial impact on results because it is an acute study.
	Metric 8:	Consistency of Exposure Administration	Medium	It appears injection volumes varied based on dosing, rather than being held constant making comparisons across doses more difficult.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Dosing was clearly reported. Analytical measurements were not performed.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose/concentration spacing were explicitly justified by study authors to minimize the number of animals used.
	Metric 12:	Exposure Route and Method	Medium	The study used a non-standard route of exposure (intratracheal injection).
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	Medium	Sex and age were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported to evaluate whether husbandry was adequate or whether there were differences between the control and exposed populations. These deficiencies are likely to have a substantial impact on results.
	Metric 15:	Number of Animals per Group	Medium	Single animals were used for each dose. This was appropriate for the study type.

**Study Citation:** Dow Chemical, (1989). Comparison of the acute lethality of selected hydrocarbons via intratracheal and oral routes (final report) with attachments, cover

sheets and letter dated 061989. Mortality

Health

**Outcome(s): Reported Health** 

Mortality

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single intratracheal injection

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 2799602

Domain		Metric	Rating	Comments
Domain 5: Outcome Ass	essment			
	Metric 16:	Outcome Assessment Methodology	Medium	Animals were observed for mortality for 3 days. This is shorter than the typical 14-day observation period specified in most acute toxicity guidelines.
	Metric 17:	Consistency of Outcome Assessment	High	Animals were consistently assessed across groups.
	Metric 18:	Sampling Adequacy	High	Single animals were used per dose group, and each animal was monitored for mortality.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for the study type.
	Metric 20:	Negative Control Response	High	None of the control animals died.
Domain 6: Confounding	/ Variable Cor Metric 21:	ntrol Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical methods are not necessary for this study type.
	Metric 24:	Reporting of Data	Medium	Mortality data were provided, but the time of death was not specifically reported for each individual chemical; instead, a general statement was made indicating that in most cases, animals died within 10 seconds.

## **Overall Quality Determination**

### Medium

HERO ID: 2799602 Table: 2 of 2

**Study Citation:** Dow Chemical, (1989). Comparison of the acute lethality of selected hydrocarbons via intratracheal and oral routes (final report) with attachments, cover

sheets and letter dated 061989. Lung/Respiratory

Health

**Outcome(s):** 

**Reported Health** Necropsy with particular attention to the lung

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single intratracheal injection

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 2799602

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	The test substance was identified as ethylene dichloride. The CASRN (107-06-2) was provided.
	Metric 2:	Test Substance Source	Low	A commercial source was named, but a lot and/or batch number was not provided.
	Metric 3:	Test Substance Purity	High	The grade was reported as ACS (American Chemical Society). The company website claims this is $99\%$ pure.
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	High	The study included surgical controls that were injected with saline. It is unclear that saline was used as a vehicle. The control animals were injected with 1 or 2 times the maximal volume of the test sustance.
	Metric 5:	Positive Controls	N/A	Positive controls are not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Characterization			
Bollium 3. Exposure	Metric 7:	Preparation and Storage of Test Substance	Medium	Information on preparation was limited; it isn't specifically indicated whether a vehicle was used. Information on storage was not reported, but this is unlikely to have a substantial impact on results because it is an acute study.
	Metric 8:	Consistency of Exposure Administration	Medium	It appears injection volumes varied based on dosing, rather than being held constant making comparisons across doses more difficult.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Dosing was clearly reported. Analytical measurements were not performed.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose/concentration spacing were explicitly justified by study authors to minimize the number of animals used.
	Metric 12:	Exposure Route and Method	Medium	The study used a non-standard route of exposure (intratracheal injection).
Domain 4: Test Anim	als			
	Metric 13:	Test Animal Characteristics	Medium	Sex and age were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported to evaluate whether husbandry was adequate and whether differences in husbandry may have occurred between control and exposed populations. These deficiencies are likely to have a substantial impact on results.
	Metric 15:	Number of Animals per Group	Medium	Single animals were used for each dose. This was appropriate for the study type.

Domain 5: Outcome Assessment

		continu	ied from previ	ous page		
Study Citation:		cal, (1989). Comparison of the acute lethality	y of selected hy	drocarbons via intratracheal and oral routes (final report) with attachments, cover		
Health	Lung/Respiratory (s):					
Outcome(s):						
Reported Health						
Effect(s):						
Duration:	Acute (less than or equal to 24 hr) Single intratracheal injection 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
Chemical:						
HERO ID:	2799602					
Domain		Metric	Rating	Comments		
	Metric 16:	Outcome Assessment Methodology	Medium	Animals were necropsied after spontaneous death, or after a 3-day observation period. This is shorter than the typical 14-day observation period specified in most acute toxicit guidelines.		
	Metric 17:	Consistency of Outcome Assessment	High	Animals were consistently assessed across groups.		
	Metric 18:	Sampling Adequacy	High	Only single animals were used per dose group, and each animal was necropsied.		
	Metric 19:	Blinding of Assessors	N/A	Blinding of assessors is not necessary for the study type.		
	Metric 20:	Negative Control Response	Medium	The study stated that the surgical procedure resulted in no major changes in controls. It was, however, noted that control animals showed minor to moderate pathology, that wa also described in the treated animals. One control animal did not have a catheter present		
Domain 6: Confoundi	ing / Variable Co	ntrol				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.		
	Metric 23:	Data Presentation and Analysis	N/A	Statistical methods are not necessary for the study type.		
	Metric 24:	Reporting of Data	High	Necropsy results were adequately presented for each animal.		

## **Overall Quality Determination**

## Medium

HERO ID: 5447286 Table: 1 of 1

Study Citation: Health		cal, (1962). Topical application of various so	olvents and	solutions to evaluate dermal irritation.			
Outcome(s): Reported Health Effect(s):	Skin/Connec	ctive Tissue: Skin irritation; Irritation: Skin	irritation;				
Duration: Chemical: HERO ID:		Acute (less than or equal to 24 hr) 14 day 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 5447286					
Domain		Metric	Rating	Comments			
Domain 1: Test Substance	ce						
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively by name within the test report.			
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was reported; however, the batch/lot number was not provided. The chemical identity was not certified by the source in the publication and could not be verified on the manufacturer's website.			
	Metric 3:	Test Substance Purity	Low	All Outcomes: The purity or grade of the test substance was not reported.			
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: The study authors reported using an appropriate, concurrent negative			
	Wietire 1.	regulive and venicle controls	Low	control group for the study type; however, details on treatment of the negative control were not adequately reported.			
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control was not included in the study and is not required for this study type			
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.			
Domain 3: Exposure Ch	aracterization						
Zomani et Zinpoodi e en	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Deficiencies in reporting of test substance preparation for exposure and storage conditions (e.g., of stock test substance, and if solutions were prepared and not used immediately) were not reported.			
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of the exposure administration were insufficiently reported and the missing information is likely to have a substantial impact on results. It is unknown if the exposures were administered similarly across animals based on insufficient details provided regarding exposures.			
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: There were deficiencies in reporting of the administered doses/concentrations (e.g., how many skin sites per animal). The exposure doses/concentrations or amounts of test substance were reported, but with substantial ambiguity about precision. Although it was reported that each skin site was treated with 10 cc of test substance, it is not stated if test substance was used neat or diluted.			
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Minor limitations in exposure frequency and duration of exposure (e.g., whether animals were treated on multiple days or only once) were identified; however, observation timepoints are reported (5 days, 8 days, 14 days).			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose/concentration spacing were not explicitly justified by study authors (e.g., based on study type, based on data from another study); however, the study identified effects for the outcome of interest and a single exposure level is acceptable based on standard guidelines for the study type.			
		Contin	nued on nex	at page			

## Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Dow Chemical, (1962). Topical application of various solvents and solutions to evaluate dermal irritation.

Health Skin/Connective Tissue; Irritation;

Outcome(s):

Reported Health

Skin/Connective Tissue: Skin irritation; Irritation: Skin irritation;

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 14 day **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447286

HERO ID:	5447286			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route and method were reported and were suited to the test substance for the outcome of interest.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Low	All Outcomes: The source, sex, age, and starting body weight of the test animal were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not sufficiently reported to allow an evaluation of whether husbandry conditions were adequate. These deficiencies are likely to have a substantial impact on results.
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals per study group was not reported.
Domain 5: Outcome A	ssessment			
Domain 3. Outcome 71	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessments for different animals) were limited, and these deficiencies are likely to have a substantial impact on results.
	Metric 18:	Sampling Adequacy	Medium	All Outcomes: Minor limitations were identified in the sampling of the outcome of interest (e.g., exact methodology for sampling/observing treatment sites was not reported) that are unlikely to have a substantial impact on results.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not required for the endpoint evaluated
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological responses of the negative controls (untreated skin sites) were not reported.
Domain 6: Confoundin	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, the reported information did not identify differences in confounding factors among treated animals.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information provided to either support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis is not required for this type of study and outcome based on current/standard guidelines.
	Metric 24:	Reporting of Data	Low	All Outcomes: The study report does not provide tabulated results/ratings for each individual animal. A single, averaged rating (e.g., bad, fair) is provided for each observation timepoint (5 days, 8 days, 14 days).

HERO ID: 5447286 Table: 1 of 1

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

... continued from previous page

**Study Citation:** Dow Chemical, (1962). Topical application of various solvents and solutions to evaluate dermal irritation.

**Health** Skin/Connective Tissue; Irritation;

**Outcome(s):** 

**Reported Health** Skin/Connective Tissue: Skin irritation; Irritation: Skin irritation;

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 14 day **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447286

Domain Metric Rating Comments

Overall Quality Determination Low

**Study Citation:** 

Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

**Effect(s):** 

Acute (less than or equal to 24 hr) Gavage **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 625286

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2 dichloroethane.
	Metric 2:	Test Substance Source	High	The source of the test substance was Occidental Chemical Corporation, Dallas, TX (batch # 303MICHIGA).
	Metric 3:	Test Substance Purity	High	Purity was 99.9%; determined by GC/thermal conductivity detection.
Domain 2: Test Design				
Boniam 2. Test Besign	Metric 4:	Negative and Vehicle Controls	Low	A negative control was included, however not all conditions were the same. Exposed animals were sacrificed at various times after exposure, the control animals were not sacrificed at every timepoint (only prior to and one time point after) along with exposed animals. Controls were sacrificed prior to and one time point after.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	"Animals were randomly assigned to treatment groups using a computer-driven program that minimized the differences between mean body weights".
D : 4 E				
Domain 3: Exposure Ch		Dramanation and Stanger of Test	High	The translation of the same of the desired
	Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation and storage was fully described.
	Metric 8:	Consistency of Exposure Administration	High	Exposures were administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for aim of the study.
	Metric 11:	Number of Exposure Groups and	Medium	Only one dose/concentration was studied. Therefore, both a NOAEL and LOAEL were
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	not obtained. The study based the dose/concentration on previous toxicity information. The route (gayage) was appropriate for test substance.
		Zinposare reduce and ritemod		The route (garage) was appropriate for test outstands
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were adequately reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was adequate for this study type (n=3).
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome methodology (Body weight) was assessed appropriately.
	Metric 17:	Consistency of Outcome Assessment	High	Assessment protocol was consistent across study groups.
		G	nued on nex	

HERO ID: 625286 Table: 1 of 2

### ... continued from previous page

**Study Citation:** Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats. Nutritional/Metabolic

Health

**Outcome(s):** 

Body weight Reported Health

Effect(s): **Duration:** 

Chemical:

Acute (less than or equal to 24 hr) Gavage 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 625286

Domain	Metric	Rating	Comments
Metric 1	3: Sampling Adequacy	High	Sampling was adequate; all animals were accounted for.
Metric 1	P: Blinding of Assessors	N/A	Blinding was not necessary for body weight.
Metric 2	): Negative Control Response	High	Biological response of negative control was appropriate.
Domain 6: Confounding / Variable	Control		
Metric 2	: Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding. Food intake was not reported.
Metric 2	2: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Metric 2	B: Data Presentation and Analysis	High	Statistical analysis was not performed, but study provided sufficient data for independent statistics.
Metric 2	l: Reporting of Data	High	Data were fully reported with individual animal data.

## **Overall Quality Determination**

## High

HERO ID: 625286 Table: 2 of 2

**Study Citation:** 

Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Inhalation **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 625286

HERO ID.	023200			
Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2 dichloroethane.
	Metric 2:	Test Substance Source	High	The source of the test substance was Occidental Chemical Corporation, Dallas, TX (batch # 303MICHIGA).
	Metric 3:	Test Substance Purity	High	Purity was 99.9%; determined by GC/thermal conductivity detection.
Domain 2: Test Design				
2 100 200g.	Metric 4:	Negative and Vehicle Controls	Uninformative	A negative control was included, however not all conditions were the same. Exposed animals were sacrificed at various times after exposure, the control animals were not sacrificed at every timepoint (only prior to and one time point after) along with exposed animals. Controls were sacrificed prior to and one time point after.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	"Animals were randomly assigned to treatment groups using a computer-driven program that minimized the differences between mean body weights".
Domain 3: Exposure Ch	aracterization			
1	Metric 7:	Preparation and Storage of Test	High	Test substance preparation and storage was fully described.
	Metric 8:	Substance Consistency of Exposure Administration	High	Exposures were administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity. For inhalation, nominal and actual concentration were reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for aim of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only one dose/concentration was studied. Therefore, both a NOAEL and LOAEL were not obtained. The study based the dose/concentration on previous toxicity information.
	Metric 12:	Exposure Route and Method	High	For inhalation, a nose-only chamber was used with airflow maintained at 60L/minute.
Domain 4: Test Animals	1			
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported.
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Medium	The number of animals/group was adequate for this study type (n=3).
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome methodology (Body weight) was assessed appropriately.
	Metric 17:	Consistency of Outcome Assessment	High	Assessment protocol was consistent across study groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate; all animals were accounted for.
			nued on next pag	

**Study Citation:** 

Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Inhalation **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 625286

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for body weight.
	Metric 20:	Negative Control Response	High	Biological response of negative control was appropriate.
Domain 6: Confounding	/ Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The test substance is a respiratory irritant. The study did not report respiratory rate. Food intake was not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed, but study provided sufficient data for independent statistics.
	Metric 24:	Reporting of Data	High	Data were fully reported with individual animal data.

## **Overall Quality Determination**

## High

**Study Citation:** Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Health

Mortality

**Outcome(s):** 

**Reported Health** Mortality

**Effect(s):** 

Acute (less than or equal to 24 hr) Acute toxicity - 8 hrs **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6570013

HERO ID.	03/0013			
Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	Identified by name as 1,2-dichlorethane; or ethylene dichloride. The CASRN was provided in an Appendix (pg. 640)
	Metric 2:	Test Substance Source	High	The supplier and batch number were provided along with confirmation of purity/characterization.
	Metric 3:	Test Substance Purity	High	Purity = 99.9%, determined by GC
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	Control animals were exposed to air-only.
	Metric 5:	Positive Controls	Medium	The study provided non-concurrent positive control data in Appendix D. Demonstration of the laboratories ability to perform the protocols is acceptable and concurrent positive controls are not required.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were "stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study."
Domain 3: Exposure Ch	aracterization			
Domain 3. Exposure Cir	Metric 7:	Preparation and Storage of Test Substance	High	The method and equipment used to generate the test substance as a vapor was reported and appropriate.
	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner
	Metric 9:	Reporting of Doses/Concentrations	High	Target, nominal, and analytical concentrations were reported. The study authors provided justification for the selected exposure concentrations.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequencies and duration were clearly reported and justified by the study author
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups were adequate for the purposes of the study and the concentrations/spacing was justified by the study authors.
	Metric 12:	Exposure Route and Method	Medium	Animals were exposed to vapors, whole-body. The dynamic chamber had 11-15 air changes/hr (depending on which chamber was used)
Domain 4: Test Animals				
Domain 4: Test Animais	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, source, and starting body weight were reported. Justification for the use of this strain was provided by the study authors.
	Metric 14:	Adequacy and Consistency of Animal	High	All animal husbandry conditions were provided in detail and were consistent and ade-

**Study Citation:** Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Health

Mortality

**Outcome(s):** 

**Reported Health** 

1

Mortality

Effect(s): Duration:

Acute (less than or equal to 24 hr) Acute toxicity - 8 hrs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6570013

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group was consistent with the guideline used.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this outcome of interest.
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).
Domain 6: Confoundir	ıg / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Respiratory rate was not reported and the test material may be a respiratory irritant. GHS hazard: H335
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis not required (no mortality observed)
	Metric 24:	Reporting of Data	High	Negative findings were reported qualitatively or quantitatively.

## **Overall Quality Determination**

## High

Study Citation: Health	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010). Lung/Respiratory; Nutritional/Metabolic; Lung/Respiratory; Nutritional/Metabolic; Neurological/Behavioral; Lung/Respiratory: Histopathology of the upper and lower respiratory tract, lung weight, BAL, gross necropsy of lung, larynx, trachea, nasal tissue;								
Outcome(s):									
Reported Health									
Effect(s):	Nutritional/Metabolic: Body weights; Lung/Respiratory: Histopathology of the upper and lower respiratory tract, lung weight, BAL, gross necropsy of								
				ca examination in the 4-hr neurotoxicity study.; Nutritional/Metabolic: Body weights;					
	•			atical signs, FOB, including hand-held and open-field observations, grip performance, athological evaluations (gross and histopathological examinations) All studies: Brain					
	C			amological evaluations (gross and instopathological examinations)All studies: Brain					
<b>Duration:</b>	weight, and gross examinations of neurological tissues); Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs								
Chemical:		bethane- Isomer: 1,2-Dichloroethane							
HERO ID:	6570013								
Domain		Metric	Rating	Comments					
Domain 1: Test Substan									
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name as 1,2-dichlorethane; or ethylene dichloride. The CASRN was provided in an Appendix (pg. 640)					
	Metric 2:	Test Substance Source	High	All Outcomes: The supplier and batch number were provided along with confirmation of purity/characterization.					
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity = 99.9%, determined by GC					
Domain 2: Test Design									
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals were exposed to air-only.					
	Metric 5:	Positive Controls	Medium	All Outcomes: The study provided non-concurrent positive control data in Appendix D. Demonstration of the laboratories ability to perform the protocols is acceptable and concurrent positive controls are not required.					
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were "stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study."					
Domain 3: Exposure Ch	aracterization								
Domain J. Exposure Cir	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The method and equipment used to generate the test substance as a vapor was reported and appropriate.					

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Study Citation: Health Outcome(s):	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010). Lung/Respiratory; Nutritional/Metabolic; Lung/Respiratory; Ocular/Sensory; Nutritional/Metabolic; Neurological/Behavioral;						
Reported Health Effect(s):  Duration: Chemical:	Lung/Respiratory: Histopathology of the upper and lower respiratory tract, lung weight, BAL, gross necropsy of lung, larynx, trachea, nasal tissue; Nutritional/Metabolic: Body weights; Lung/Respiratory: Histopathology of the upper and lower respiratory tract, lung weight, BAL, gross necropsy of lung, larynx, trachea, nasal tissue; Ocular/Sensory: Ophthalmologica examination in the 4-hr neurotoxicity study.; Nutritional/Metabolic: Body weights; Neurological/Behavioral: In the 4-hr neurotox study: Detailed clinical signs, FOB, including hand-held and open-field observations, grip performance, landing foot splay, rectal temperature, and motor activity, Neuropathological evaluations (gross and histopathological examinations)All studies: Brain weight, and gross examinations of neurological tissues); Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:  Domain	6570013	Metric	Rating	Comments			
Domain	Metric 8:	Consistency of Exposure Administration	Low	Lung/Respiratory: The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.; Nutritional/Metabolic: The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.; Lung/Respiratory: The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.; Ocular/Sensory: There is some ambiguity surrounding exposure. See Table 1 pg. 80/683. Exposures were conducted on 4 separate days. Each day purportedly had a "counterbalanced number of rats/sex/dose", but the actual numbers of animals/sex/concentration were included on each separate day.; Nutritional/Metabolic: There is some ambiguity surrounding exposure. See Table 1 pg. 80/683. Exposures were conducted on 4 separate days. Each day purportedly had a "counterbalanced number of rats/sex/dose", but the actual numbers of animals/sex/concentration were included on each separate day.; Neurological/Behavioral: There is some ambiguity surrounding exposure. See Table 1 pg. 80/683. Exposures were conducted on 4 separate days. Each day purportedly had a "counterbalanced number of rats/sex/dose", but the actual numbers of animals/sex/concentration were included on each separate days. Fach day purportedly had a "counterbalanced number of rats/sex/dose", but the actual numbers of animals/sex/concentration were included on each separate days.			
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target, nominal, and analytical concentrations were reported. The study authors provided justification for the selected exposure concentrations.			
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequencies and duration were clearly reported and justified by the study author			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups were adequate for the purposes of the study and the concentrations/spacing was justified by the study authors.			
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Animals were exposed to vapors, whole-body. The dynamic chamber had 11-15 air changes/hr (depending on which chamber was used)			
Domain 4: Test Animals	S						
	Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, age, source, and starting body weight were reported. Justification for the use of this strain was provided by the study authors.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All animal husbandry conditions were provided in detail and were consistent and adequate for the purposes of the study.			
		Contin	nued on nex	ct page			

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				Tevious page		
Study Citation:				loride; final report (docket no . OPPT-2003-0010).		
Health Outcome(s):	Lung/Respir	atory; Nutritional/Metabolic; Lung/Respira	atory; Ocular	/Sensory; Nutritional/Metabolic; Neurological/Behavioral;		
Reported Health Effect(s):	Lung/Respiratory: Histopathology of the upper and lower respiratory tract, lung weight, BAL, gross necropsy of lung, larynx, trachea, nasal tissue; Nutritional/Metabolic: Body weights; Lung/Respiratory: Histopathology of the upper and lower respiratory tract, lung weight, BAL, gross necropsy of lung, larynx, trachea, nasal tissue; Ocular/Sensory: Ophthalmologica examination in the 4-hr neurotoxicity study.; Nutritional/Metabolic: Body weights; Neurological/Behavioral: In the 4-hr neurotox study: Detailed clinical signs, FOB, including hand-held and open-field observations, grip performance, landing foot splay, rectal temperature, and motor activity, Neuropathological evaluations (gross and histopathological examinations)All studies: Brain weight, and gross examinations of neurological tissues);					
Duration:		han or equal to 24 hr) Acute toxicity - 4 hr				
Chemical: HERO ID:		bethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
	Metric 15:	Number of Animals per Group	Medium	Lung/Respiratory: The number of animals per group was consistent with the guideline used.; Nutritional/Metabolic: The number of animals per group was consistent with the guideline used.; Lung/Respiratory: The number of animals per group was consistent with the guideline used.; Ocular/Sensory: The number of animals was consistent with OECD TG 424; Nutritional/Metabolic: The number of animals was consistent with OECD TG 424; Neurological/Behavioral: The number of animals was consistent with OECD TG 424		
Domain 5: Outcome A	Assessment					
Domain 3. Outcome A	Metric 16:	Outcome Assessment Methodology	High	Lung/Respiratory: Histology and examination of BAL fluid.; Nutritional/Metabolic: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.; Lung/Respiratory: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.; Ocular/Sensory: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.; Nutritional/Metabolic: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology addressed the intended outcome(s) of interest.; Neurological/Behavioral: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.		
	Metric 17:	Consistency of Outcome Assessment	High	Lung/Respiratory: The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.; Nutritional/Metabolic: The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.; Lung/Respiratory: The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.; Ocular/Sensory: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups; Nutritional/Metabolic: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups; Neurological/Behavioral: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups; Neurological/Behavioral: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups		
			TT' 1			
	Metric 18:	Sampling Adequacy Blinding of Assessors	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome(s) of interest		

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Study Citation: Health Outcome(s):				loride; final report (docket no . OPPT-2003-0010). /Sensory; Nutritional/Metabolic; Neurological/Behavioral;		
Reported Health Effect(s):	Lung/Respiratory: Histopathology of the upper and lower respiratory tract, lung weight, BAL, gross necropsy of lung, larynx, trachea, nasal tissue; Nutritional/Metabolic: Body weights; Lung/Respiratory: Histopathology of the upper and lower respiratory tract, lung weight, BAL, gross necropsy of lung, larynx, trachea, nasal tissue; Ocular/Sensory: Ophthalmologica examination in the 4-hr neurotoxicity study.; Nutritional/Metabolic: Body weights; Neurological/Behavioral: In the 4-hr neurotox study: Detailed clinical signs, FOB, including hand-held and open-field observations, grip performance, landing foot splay, rectal temperature, and motor activity, Neuropathological evaluations (gross and histopathological examinations)All studies: Brain weight, and gross examinations of neurological tissues);					
Duration:		gross examinations of neurological tissues); han or equal to 24 hr) Acute toxicity - 4 hrs				
Chemical: HERO ID:		pethane- Isomer: 1,2-Dichloroethane	'			
Domain	Metric		Rating	Comments		
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).		
Domain 6: Confoundi	-		_			
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Respiratory rate was not reported and the test material may be a respiratory irritant. GHS hazard: H335		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.		
	Metric 23:	Data Presentation and Analysis	High	Lung/Respiratory: Statistical methods were described and appropriate for the outcome of interest.; Nutritional/Metabolic: Statistical methods were described and appropriate for the outcome of interest.; Lung/Respiratory: Statistical methods were described and appropriate for the outcome of interest.; Ocular/Sensory: Statistical methods were described and adequate.; Nutritional/Metabolic: Statistical methods were described and adequate.; Neurological/Behavioral: Statistical methods were described and adequate.		
	Metric 24:	Reporting of Data	High	Lung/Respiratory: Detailed data tables, figures, and individual animal data were provided.; Nutritional/Metabolic: Detailed data tables, figures, and individual animal data were provided.; Lung/Respiratory: Detailed data tables, figures, and individual animal data were provided.; Ocular/Sensory: Data were adequately reported for all groups; individual animal data were provided.; Nutritional/Metabolic: Data were adequately reported for all groups; individual animal data were provided.; Neurological/Behavioral: Data were adequately reported for all groups; individual animal data were provided.		
Overall Qual	ity Detern	nination	High			

HERO ID: 6570013 Table: 3 of 7

**Study Citation:** Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010). Health Mortality; Mortality;

**Outcome(s):** 

Reported Health Mortality: Mortality; Mortality; Mortality;

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute neurotoxicity-4hrs

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HEDO ID

HERO ID:	6570013			
Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name as 1,2-dichlorethane; or ethylene dichloride. The CASRN was provided in an Appendix (pg. 640)
	Metric 2:	Test Substance Source	High	All Outcomes: The supplier and batch number were provided along with confirmation of purity/characterization.
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity = 99.9%, determined by GC
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals were exposed to air-only.
	Metric 5:	Positive Controls	Medium	All Outcomes: The study provided non-concurrent positive control data in Appendix
	wiedle 3.	rosuve controls	Wicdiani	D. Demonstration of the laboratories ability to perform the protocols is acceptable and concurrent positive controls are not required.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were "stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study."
Domain 3: Exposure Ch	aracterization			
Domain 5. Exposure Cir	Metric 7:	Preparation and Storage of Test	High	All Outcomes: The method and equipment used to generate the test substance as a vapor
	Wietife 7.	Substance	Iligii	was reported and appropriate.
	Metric 8:	Consistency of Exposure Administration	Low	Mortality: There is some ambiguity surrounding exposure. See Table 1 pg. 80/683. Exposures were conducted on 4 separate days. Each day purportedly had a "counterbalanced number of rats/sex/dose", but the actual numbers of animals/sex/concentration were included on each separate day.; Mortality: The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target, nominal, and analytical concentrations were reported. The study authors provided justification for the selected exposure concentrations.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequencies and duration were clearly reported and justified by the study author
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups were adequate for the purposes of the study and the concentrations/spacing was justified by the study authors.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Animals were exposed to vapors, whole-body. The dynamic chamber had 11-15 air changes/hr (depending on which chamber was used)
Domain 4: Test Animals				
20main 1. 10st / miniars	Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, age, source, and starting body weight were reported. Justification for the use of this strain was provided by the study authors.
		Contin	nued on nex	t page

Study Citation: Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010). Health Mortality; Mortality;

**Outcome(s):** 

Reported Health

Mortality: Mortality; Mortality; Mortality;

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute neurotoxicity-4hrs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6570013

Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All animal husbandry conditions were provided in detail and were consistent and adequate for the purposes of the study.
	Metric 15:	Number of Animals per Group	Medium	Mortality: The number of animals was consistent with OECD TG 424; Mortality: The number of animals per group was consistent with the guideline used.
Domain 5: Outcome A	ssessment			
Johnan J. Odcome 1	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Mortality: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups; Mortality: The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome(s) of interest
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this outcome of interest.
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).
Domain 6: Confoundir	ng / Variable Coi	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Respiratory rate was not reported and the test material may be a respiratory irritant. GHS hazard: H335
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis not required (no mortality observed)
	Metric 24:	Reporting of Data	High	All Outcomes: Negative findings were reported qualitatively or quantitatively.

### **Overall Quality Determination**

### High

HERO ID: 6570013 Table: 4 of 7

**Study Citation:** 

Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weights

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Identified by name as 1,2-dichlorethane; or ethylene dichloride. The CASRN was provided in an Appendix (pg. 640)
	Metric 2:	Test Substance Source	High	The supplier and batch number were provided along with confirmation of purity/characterization.
	Metric 3:	Test Substance Purity	High	Purity = 99.9%, determined by GC
Domain 2: Test Desig	n			
Domain 2. Test Desig	Metric 4:	Negative and Vehicle Controls	High	Control animals were exposed to air-only.
	Metric 5:	Positive Controls	Medium	The study provided non-concurrent positive control data in Appendix D. Demonstration of the laboratories ability to perform the protocols is acceptable and concurrent positive controls are not required.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were "stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study."
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	High	The method and equipment used to generate the test substance as a vapor was reported and appropriate.
	Metric 8:	Consistency of Exposure Administration	Low	The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.
	Metric 9:	Reporting of Doses/Concentrations	High	Target, nominal, and analytical concentrations were reported. The study authors provided justification for the selected exposure concentrations.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequencies and duration were clearly reported and justified by the study author
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups were adequate for the purposes of the study and the concentrations/spacing was justified by the study authors.
	Metric 12:	Exposure Route and Method	Medium	Animals were exposed to vapors, whole-body. The dynamic chamber had 11-15 air changes/hr (depending on which chamber was used)
Domain 4: Test Anim	als			
Zoman ii Test I IIIII	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, source, and starting body weight were reported Justification for the use of this strain was provided by the study authors.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All animal husbandry conditions were provided in detail and were consistent and adequate for the purposes of the study.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group was consistent with the guideline used.

**Study Citation:** Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights

Effect(s):
Duration:

Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
Metric 17:	Consistency of Outcome Assessment	Medium	The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.
Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the $outcome(s)$ of interest
Metric 19:	Blinding of Assessors	N/A	Not necessary for this outcome of interest.
Metric 20:	Negative Control Response	Low	weight loss was also reported in the control group, which makes body weight data diffi- cult to interpret
Domain 6: Confounding / Variable Co	ntrol		
Metric 21:	Confounding Variables in Test Design	Low	Respiratory rate was not reported and the test material may be a respiratory irritant.
	and Procedures		GHS hazard: H335
Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	
Metric 22: Metric 23:	Health Outcomes Unrelated to	Medium High	GHS hazard: H335  There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure

Study Citation:	Dow Chemical, (2006), R.	e: Testing consent order for ethylene dichloride: final report (docke	t no . OPPT-2003-0010).

Health

Neurological/Behavioral

**Outcome(s):** 

**Effect(s):** 

**Reported Health** In the 4-hr neurotox study: Detailed clinical signs, FOB, including hand-held and open-field observations, grip performance, landing foot splay, rectal temperature, and motor activity, Neuropathological evaluations (gross and histopathological examinations) All studies: Brain weight, and gross examinations

of neurological tissues)

Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs **Duration:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

HERO ID: 6570013

HERO ID:	6570013			
Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Identified by name as 1,2-dichlorethane; or ethylene dichloride. The CASRN was provided in an Appendix (pg. 640)
	Metric 2:	Test Substance Source	High	The supplier and batch number were provided along with confirmation of purity/characterization.
	Metric 3:	Test Substance Purity	High	Purity = 99.9%, determined by GC
Domain 2: Test Design				
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	Uigh	Control animals were exposed to air-only.
	Metric 5:	Positive Controls	High Medium	•
	Metric 3:	rositive Colitions	wiedium	The study provided non-concurrent positive control data in Appendix D. Demonstration of the laboratories ability to perform the protocols is acceptable and concurrent positive controls are not required.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were "stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study."
Domain 3: Exposure Cl	haracterization			
Domain 5. Exposure Ci	Metric 7:	Preparation and Storage of Test	High	The method and equipment used to generate the test substance as a vapor was reported
	metric 7.	Substance	111511	and appropriate.
	Metric 8:	Consistency of Exposure	Low	The 4-hr 50 ppm exposure group was added on at a later time point, and was not done
		Administration		concurrently with the other 4-hr exposure groups.
	Metric 9:	Reporting of Doses/Concentrations	High	Target, nominal, and analytical concentrations were reported. The study authors provided justification for the selected exposure concentrations.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequencies and duration were clearly reported and justified by the study author
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups were adequate for the purposes of the study and the concentrations/spacing was justified by the study authors.
	Metric 12:	Exposure Route and Method	Medium	Animals were exposed to vapors, whole-body. The dynamic chamber had 11-15 air changes/hr (depending on which chamber was used)
Damain 4. Test Assissed				
Domain 4: Test Animal		T-+ A -: 1 Ch	TT: _1.	
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, source, and starting body weight were reported. Justification for the use of this strain was provided by the study authors.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All animal husbandry conditions were provided in detail and were consistent and adequate for the purposes of the study.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group was consistent with the guideline used.

#### Continued on next page ...

		conun	ueu iroin p	revious page			
Study Citation: Health	Dow Chemic Neurologica		hylene dich	oride; final report (docket no . OPPT-2003-0010).			
Outcome(s):							
Reported Health	In the 4-hr n	eurotox study: Detailed clinical signs, FOB,	including h	and-held and open-field observations, grip performance, landing foot splay, rectal tem-			
Effect(s):	perature, and	d motor activity, Neuropathological evaluati	ions (gross a	and histopathological examinations)All studies: Brain weight, and gross examinations			
	of neurologi	· · · · · · · · · · · · · · · · · · ·					
Duration:		than or equal to 24 hr) Acute toxicity - 4 hrs					
Chemical:		1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	6570013						
Domain		Metric	Rating	Comments			
Domain 5: Outcome A	Assessment						
	Metric 16:	Outcome Assessment Methodology	Low	clinical observations only			
	Metric 17:	Consistency of Outcome Assessment	High	The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.			
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest			
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this outcome of interest.			
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).			
Domain 6: Confoundi	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Respiratory rate was not reported and the test material may be a respiratory irritant. GHS hazard: H335			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described and appropriate for the outcome of interest.			
	Metric 24:	Reporting of Data	High	Detailed data tables, figures, and individual animal data were provided.			
Overall Qual	lity Deterr	mination	High				

Study Citation:
Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Health
Renal/Kidney; Hepatic/Liver; Ocular/Sensory;
Outcome(s):

**Reported Health**Renal/Kidney: Kidney histopathology and organ weight; Hepatic/Liver: Liver histopathology and organ weight.; Hepatic/Liver: Liver histopathology and organ weight.; Hepatic/Liver: Liver histopathology and organ weight.; Ocular/Sensory: Ophthalmologica examination in the 4-hr neurotoxicity study.;

**Duration:** Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6570013

HERO ID:	03/0013			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name as 1,2-dichlorethane; or ethylene dichloride. The CASRN was provided in an Appendix (pg. 640)
	Metric 2:	Test Substance Source	High	All Outcomes: The supplier and batch number were provided along with confirmation of purity/characterization.
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity = 99.9%, determined by GC
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals were exposed to air-only.
	Metric 5:	Positive Controls	Medium	All Outcomes: The study provided non-concurrent positive control data in Appendix D. Demonstration of the laboratories ability to perform the protocols is acceptable and
				concurrent positive controls are not required.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were "stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study."
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The method and equipment used to generate the test substance as a vapor was reported and appropriate.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target, nominal, and analytical concentrations were reported. The study authors provided justification for the selected exposure concentrations.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequencies and duration were clearly reported and justified by the study author
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups were adequate for the purposes of the study and the concentrations/spacing was justified by the study authors.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Animals were exposed to vapors, whole-body. The dynamic chamber had 11-15 air changes/hr (depending on which chamber was used)
Domain 4: Test Animals				
Domain 4: Test Animais		Test Animal Characteristics	High	All Outcomes The test spirits are in a second spirit and a second spirit and a second spirit are spirits and a second spirits are spirits as a second spirit and a second spirits are spirits as a second spirit are spir
	Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, age, source, and starting body weight were reported. Justification for the use of this strain was provided by the study authors.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All animal husbandry conditions were provided in detail and were consistent and adequate for the purposes of the study.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals per group was consistent with the guideline used.

#### Continued on next page ...

		contin	ued from p	revious page			
Study Citation: Health Outcome(s):		Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010). Renal/Kidney; Hepatic/Liver; Hepatic/Liver; Ocular/Sensory;					
Reported Health Effect(s): Duration: Chemical: HERO ID:	Renal/Kidney: Kidney histopathology and organ weight; Hepatic/Liver: Liver histopathology and organ weight.; Hepatic/Liver: Liver histopathology and organ weight.; Ocular/Sensory: Ophthalmologica examination in the 4-hr neurotoxicity study.; Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 6570013						
Domain		Metric Rating Comments					
Domain 5: Outcome A	Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	Renal/Kidney: The study did not include clinical chemistry evaluations, but the most sensitive endpoint (histopathology); Hepatic/Liver: The study did not include clinical chemistry evaluations, but the most sensitive endpoint (histopathology); Hepatic/Liver: Histopathology only was performed; Ocular/Sensory: Ophthalmological examinations were performed			
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.			
	Metric 18:	Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome(s) of interest			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this outcome of interest.			
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).			
Domain 6: Confoundi	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Respiratory rate was not reported and the test material may be a respiratory irritant. GHS hazard: H335			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were described and appropriate for the outcome of interest.			
	Metric 24:	Reporting of Data	High	All Outcomes: Detailed data tables, figures, and individual animal data were provided.			
Overall Qual	ity Detern	nination	High				

Study Citation: Health Outcome(s): Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Adrenals (Adrenals); Necropsy (Gross necropsy of multiple organs and tissues); Necropsy (Gross necropsy of multiple tissues); Necropsy (Gross necropsy);

Reported Health Effect(s):

Adrenals (Adrenals): Adrenal organ weights; Necropsy (Gross necropsy of multiple organs and tissues): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea; Necropsy (Gross necropsy of multiple tissues): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea; Necropsy (Gross necropsy): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea;

Duration: Chemical: HERO ID: Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 6570013

Domain Rating Comments Metric Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: Identified by name as 1,2-dichlorethane; or ethylene dichloride. The CASRN was provided in an Appendix (pg. 640) Metric 2: Test Substance Source High All Outcomes: The supplier and batch number were provided along with confirmation of purity/characterization. Metric 3: **Test Substance Purity** High All Outcomes: Purity = 99.9%, determined by GC Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: Control animals were exposed to air-only. Metric 5: Positive Controls Medium All Outcomes: The study provided non-concurrent positive control data in Appendix D. Demonstration of the laboratories ability to perform the protocols is acceptable and concurrent positive controls are not required. Metric 6: Randomized Allocation of Animals Medium All Outcomes: Animals were "stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study." Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test High All Outcomes: The method and equipment used to generate the test substance as a vapor was reported and appropriate. Substance Metric 8: Consistency of Exposure Low Adrenals (Adrenals): The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.; Necropsy Administration (Gross necropsy of multiple organs and tissues): The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.; Necropsy (Gross necropsy of multiple tissues): The 4-hr 50 ppm exposure group was added on at a later time point, and was not done concurrently with the other 4-hr exposure groups.; Necropsy (Gross necropsy): There is some ambiguity surrounding exposure. See Table 1 pg. 80/683. Exposures were conducted on 4 separate days. Each day purportedly had a "counterbalanced number of rats/sex/dose", but the actual numbers of animals/sex/concentration were included on each separate day. Metric 9: Reporting of Doses/Concentrations High All Outcomes: Target, nominal, and analytical concentrations were reported. The study authors provided justification for the selected exposure concentrations.

**Study Citation:** Health Outcome(s): Reported Health

Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Adrenals (Adrenals); Necropsy (Gross necropsy of multiple organs and tissues); Necropsy (Gross necropsy of multiple tissues); Necropsy (Gross necropsy);

Effect(s):

Adrenals (Adrenals): Adrenal organ weights; Necropsy (Gross necropsy of multiple organs and tissues): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea; Necropsy (Gross necropsy of multiple tissues): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea; Necropsy (Gross necropsy): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea;

**Duration:** Chemical: **HERO ID:**  Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

6570013

Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequencies and duration were clearly reported and justified by the study author
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups were adequate for the purposes of the study and the concentrations/spacing was justified by the study authors.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Animals were exposed to vapors, whole-body. The dynamic chamber had 11-15 air changes/hr (depending on which chamber was used)
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, age, source, and starting body weight were reported. Justification for the use of this strain was provided by the study authors.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All animal husbandry conditions were provided in detail and were consistent and adequate for the purposes of the study.
	Metric 15:	Number of Animals per Group	Medium	Adrenals (Adrenals): The number of animals per group was consistent with the guide-line used.; Necropsy (Gross necropsy of multiple organs and tissues): The number of animals per group was consistent with the guideline used.; Necropsy (Gross necropsy of multiple tissues): The number of animals per group was consistent with the guideline used.; Necropsy (Gross necropsy): The number of animals was consistent with OECD TG 424
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Uninformative	Adrenals (Adrenals): Organ weight only was assessed.; Necropsy (Gross necropsy of multiple organs and tissues): Several organs/tissues were subjected to gross examinations only, which is not considered sensitive for assessment of toxicity of these organs.; Necropsy (Gross necropsy of multiple tissues): Several organs/tissues were subjected to gross examinations only, which is not considered sensitive for assessment of toxicity of these organs.; Necropsy (Gross necropsy): Several organs/tissues were only grossly examined; this is not considered sensitive for assessment of toxicity of these organ systems.

Study Citation: Health Outcome(s): Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Adrenals (Adrenals); Necropsy (Gross necropsy of multiple organs and tissues); Necropsy (Gross necropsy of multiple tissues); Necropsy (Gross necropsy);

Reported Health Effect(s):

Adrenals (Adrenals): Adrenal organ weights; Necropsy (Gross necropsy of multiple organs and tissues): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea; Necropsy (Gross necropsy of multiple tissues): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea; Necropsy (Gross necropsy): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea;

Duration: Chemical:

Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments
Metric 17:	Consistency of Outcome Assessment	High	Adrenals (Adrenals): The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.; Necropsy (Gross necropsy of multiple organs and tissues): The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.; Necropsy (Gross necropsy of multiple tissues): The same protocol was used across study groups. Except for the 4-hr 50 ppm group, all groups were concurrently assessed.; Necropsy (Gross necropsy): Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups
Metric 18:	Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome(s) of interest
Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this outcome of interest.
Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).
Domain 6: Confounding / Variable Con	ntrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Respiratory rate was not reported and the test material may be a respiratory irritant. GHS hazard: H335
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	High	Adrenals (Adrenals): Statistical methods were described and appropriate for the outcome of interest.; Necropsy (Gross necropsy of multiple organs and tissues): Statistical methods were described and appropriate for the outcome of interest.; Necropsy (Gross necropsy of multiple tissues): Statistical methods were described and appropriate for the outcome of interest.; Necropsy (Gross necropsy): Statistical methods were described and adequate.

Study Citation: Health Outcome(s): Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).

Adrenals (Adrenals); Necropsy (Gross necropsy of multiple organs and tissues); Necropsy (Gross necropsy of multiple tissues); Necropsy (Gross necropsy);

Reported Health Effect(s):

Adrenals (Adrenals): Adrenal organ weights; Necropsy (Gross necropsy of multiple organs and tissues): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea; Necropsy (Gross necropsy of multiple tissues): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea; Necropsy (Gross necropsy): Gross necropsy on aorta, auditory sebaceous gland, bone, bone marrow, cecum, coagulating gland, colon, duodenum, esophagus, heart, ileum, jejunum, lacrimal gland, lymph node, mediastinal tissue, mesenteric tissue, oral tissue, pancreas, parathyroid gland, pituitary gland, rectum, salivary gland, skeletal muscle, skin and subcutis, spleen, stomach, thymus, thyroid gland, tongue, trachea;

Duration: Chemical: Acute (less than or equal to 24 hr) Acute toxicity - 4 hrs

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6570013

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	High	Adrenals (Adrenals): Detailed data tables, figures, and individual animal data were pro-
				vided.; Necropsy (Gross necropsy of multiple organs and tissues): Detailed data tables,
				figures, and individual animal data were provided.; Necropsy (Gross necropsy of mul-
				tiple tissues): Detailed data tables, figures, and individual animal data were provided.;
				Necropsy (Gross necropsy): Data were adequately reported for all groups; individual
				animal data were provided

### **Overall Quality Determination**

### Uninformative

HERO ID: 725343 Table: 1 of 2

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Study Citation: Health	Dow Chemical, (1956). Results of skin absorption studies on carbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, and chlorothene. Irritation						
Outcome(s): Reported Health	Irritation, corrosion and damage to the skin were assessed.						
Effect(s): Duration: Chemical: HERO ID:	Acute (less than or equal to 24 hr) 24 hrs - Dermal 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 725343						
Domain		Metric	Rating	Comments			
Domain 1: Test Substance	ce						
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichloroethane. A molecular and structural formula was provided. No CASRN was specified.			
	Metric 2:	Test Substance Source	Low	The chemical source was not reported and the test substance was not analytically verified.			
	Metric 3:	Test Substance Purity	Low	The purity was not reported.			
Domain 2: Test Design							
	Metric 4:	Negative and Vehicle Controls	N/A	Negative controls are not necessary for an acute toxicity test (and untreated parts of the body can be used as controls for dermal irritation studies).			
	Metric 5:	Positive Controls	N/A	Not necessary for the study type			
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups; however, this is not typically relevant for an acute toxicity study.			
Domain 2: Evnagura Ch	araatarization						
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Medium	Details of preparation and storage were not provided; however, this is unlikely to have a substantial impact on results in an acute duration study.			
	Metric 8:	Consistency of Exposure Administration	Medium	Limited details of exposure administration were provided; missing details (e.g., volume and coverage area) are not expected to have a substantial impact on results.			
	Metric 9:	Reporting of Doses/Concentrations	Medium	Doses were clearly reported. It is unclear if they are nominal or analytical.			
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration is consistent with dermal acute toxcity studies.			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups and spacing were acceptable; however, the doses tested are above those currently recommended for this study type.			
	Metric 12:	Exposure Route and Method	High	The exposure route and method were appropriate			
Domain 4: Test Animals	S						
	Metric 13:	Test Animal Characteristics	Low	Strain, sex, and starting body weights and source were not provided.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not provided.			
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group is above the required/recommended numbers in the current OECD TG 404 guideline.			
Domain 5: Outcome Ass	sessment						
		Contin	nued on nex	ct page			

HERO ID: 725343 Table: 1 of 2

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Study Citation:	Dow Chemi	cal. (1956). Results of skin absorption s	studies on c	arbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, an			
Study Citation.	chlorothene.						
Health	Irritation						
Outcome(s):							
Reported Health	Irritation, co	rrosion and damage to the skin were assesse	ed.				
Effect(s):							
Duration:	Acute (less t	han or equal to 24 hr) 24 hrs - Dermal					
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	725343						
Domain		Metric	Rating	Comments			
	Metric 16:	Outcome Assessment Methodology	Low	The methods for evaluating effects on the skin were not specified, and it is unclear whether scoring was done (e.g., Draize). It was not specified how long animals were observed following exposure (e.g., the recommended duration is 14 days), or if any of the effects were reversible.			
	Metric 17:	Consistency of Outcome Assessment	Medium	There were limited details in the execution of the outcome assessment protocol, but it is assumed all animals were consistently assessed.			
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported.			
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the study type			
	Metric 20:	Negative Control Response	N/A	Not applicable for the study type			
Di (. Cfi:	/ W:-bl- C						
Domain 6: Confoundi			T				
	Metric 21:	Confounding Variables in Test Design	Low	The study did not report information to determine whether confounding was an issue.			
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis is not necessary for the study type			
	Metric 24:	Reporting of Data	Low	No irritation scores were provided. Incidences were not provided. It is unknown if localized effects were seen on all animals or only those that died.			
Overall Qual	ity Deterr	nination	Low	ized effects were seen on all ammais or only those that died.			

Study Citation: Dow Chemical, (1956). Results of skin absorption studies on carbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, and

Health chlorothene. Mortality

**Outcome(s):** 

**Reported Health** 

Mortality

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) 24 hrs - Dermal **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	123343			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichloroethane. A molecular and structural formula was provided. No CASRN was specified.
	Metric 2:	Test Substance Source	Low	The chemical source was not reported and the test substance was not analytically verified.
	Metric 3:	Test Substance Purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	Negative controls are not necessary for an acute toxicity test.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups; however, this is not typically relevant for an acute toxicity study.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	Details of preparation and storage were not provided; however, this is unlikely to have a substantial impact on results in an acute duration study.
	Metric 8:	Consistency of Exposure Administration	Medium	Limited Details of exposure administration were provided; missing details (e.g., volume and coverage area) are not expected to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Doses were clearly reported. It is unclear if they are nominal or analytical.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration is consistent with acute dermal toxicity studies.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups and spacing were acceptable; however, the doses tested are above those currently recommended for this study type.
	Metric 12:	Exposure Route and Method	High	The exposure route and method were appropriate
Domain 4: Test Animals	3			
	Metric 13:	Test Animal Characteristics	Low	Strain, sex, and starting body weights and source were not provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not provided.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group is above the required/recommended numbers in the current OECD TG 402 guideline.
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Animals were observed for mortality; however, it was not specified how long animals were observed following exposure (e.g., the recommended duration is 14 days).
	Metric 17:	Consistency of Outcome Assessment	Medium	There were limited details in the execution of the outcome assessment protocol, but it is assumed all animals were consistently assessed.

Study Citation: Dow Chemical, (1956). Results of skin absorption studies on carbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, and

Health chlorothene. Mortality

**Outcome(s):** 

Reported Health

Mortality

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) 24 hrs - Dermal **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 725343

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the study type
	Metric 20:	Negative Control Response	N/A	Not applicable for the study type
Domain 6: Confounding	g / Variable Cor Metric 21:	ntrol Confounding Variables in Test Design and Procedures	Low	The study did not report information to determine whether confounding was an issue.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis is not necessary for the study type
	Metric 24:	Reporting of Data	Medium	The timing and cause of death was not reported.

### **Overall Quality Determination**

### Medium

HERO ID: 60771 Table: 1 of 3

**Study Citation:** Francovitch, R.J., Schor, N.A., George, W.J. (1986). Effects of SKF 525A, phenobarbital, and 3-methylcholanthrene on ethylene dichloride toxicity

following inhalation exposure. International Journal of Toxicology 5(2):117-126. Health Mortality

**Outcome(s):** 

**Reported Health** Mortality 24 and 48 hours after exposure.

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- 4 hours Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID.	00771			
Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (1,2-dichloroethane).
	Metric 2:	Test Substance Source	Low	The source of the test substance was Aldrich Chemical Co., Milwaukee, Wisconsin. The batch/lot number were not provided.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported to be >99%.
Domain 2: Test Desig	gn			
•	Metric 4:	Negative and Vehicle Controls	High	Appropriate negative control was included (air).
	Metric 5:	Positive Controls	N/A	A positive control was not required.
	Metric 6:	Randomized Allocation of Animals	Low	The authors do not report how the animals were allocated.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not provided. Given the volatility of the test substance, this information would be useful.
	Metric 8:	Consistency of Exposure Administration	High	Test substance was administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Measured concentrations were not reported. The authors do report that they were within 10% of the theoretically generated concentration.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	A NOAEL for mortality could not be determined, however a dose-response was observed.
	Metric 12:	Exposure Route and Method	Medium	Exposure route and method (head-only) were appropriate and described in detail in sited reference (Franchovitch et al. 1985). However, the number of air changes/hour were not reported.
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	Medium	Age and source of mice were not reported; however this is unlikely to have a substantial impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some husbandry conditions were reported (10 mice/cage, diet and water), all others were not reported.
		Contin	ued on next pa	age
			· r	

HERO ID: 60771 Table: 1 of 3

#### ... continued from previous page

Study Citation: Francovitch, R.J., Schor, N.A., George, W.J. (1986). Effects of SKF 525A, phenobarbital, and 3-methylcholanthrene on ethylene dichloride toxicity

following inhalation exposure. International Journal of Toxicology 5(2):117-126.

Health

Mortality

Outcome(s):

Reported Health

Mortality 24 and 48 hours after exposure.

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- 4 hours **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 60771

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The authors do not report exactly how many animals were treated/group. Figure 3 states that the 1500 ppm group contained 15 mice. Figures 1 and 2 report data from a minimum of 10 exposed mice from all dose group (except control). Table 1 (the only one with control reported) reports n=5. It can be concluded that n=5-15/ group, which is appropriate
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment and methodology were appropriate to measure outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	The sampling was adequate. For mortality a minimum of 10 animals/group.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary since the outcome was death.
	Metric 20:	Negative Control Response	Low	Authors report exposed groups had an increase in death rate compared to negative control, but do not report the number of deaths (if any) in the negative control group.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Low	Test substance is a respiratory irritant and therefore respiratory rate should be reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described and appropriate.
	Metric 24:	Reporting of Data	High	Exposure related mortality data is reported.

### **Overall Quality Determination**

### Medium

Study Citation:	Francovitch, R.J., Schor, N.A., George, W.J. (1986).	Effects of SKF 525A, phenobarbital, and	3-methylcholanthrene on ethylene dichloride toxicity

following inhalation exposure. International Journal of Toxicology 5(2):117-126.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health

Relative kidney weight and renal tubular damage (histopathology)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- 4 hours **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 60771

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (1,2-dichloroethane).
	Metric 2:	Test Substance Source	Low	The source of the test substance was Aldrich Chemical Co., Milwaukee, Wisconsin. The batch/lot number were not provided.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported to be >99%.
Domain 2: Test Desig	ŗn			
C	Metric 4:	Negative and Vehicle Controls	High	Appropriate negative control was included (air).
	Metric 5:	Positive Controls	N/A	A positive control was not required.
	Metric 6:	Randomized Allocation of Animals	Low	The authors do not report how the animals were allocated.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not provided. Given the volatility of the test substance, this information would be useful.
	Metric 8:	Consistency of Exposure Administration	High	Test substance was administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Measured concentrations were not reported. The authors do report that they were within 10% of the theoretically generated concentration.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were appropriate for an acute study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	A NOAEL for relative kidney weight and renal tubular damage could not be determined, however a dose-response was observed.
	Metric 12:	Exposure Route and Method	Medium	Exposure route and method (head-only) were appropriate and described in detail in sited reference (Franchovitch et al. 1985). However, the number of air changes/hour were not reported.
Domain 4: Test Anim	als			
20114111	Metric 13:	Test Animal Characteristics	Medium	Age and source of mice were not reported; however this is unlikely to have a substantial impact on results.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Some husbandry conditions were reported (10 mice/cage, diet and water), all others were not reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Medium	The authors do not report exactly how many animals were treated/group. Figure 3 states that the 1500 ppm group contained 15 mice. Figures 1 and 2 report data from a minimum of 10 exposed mice from all dose group (except control). Table 1 (the only one with control reported) reports n=5. It can be concluded that n=5-15/ group, which is appropriate

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Study Citation: Francovitch, R.J., Schor, N.A., George, W.J. (1986). Effects of SKF 525A, phenobarbital, and 3-methylcholanthrene on ethylene dichloride toxicity

following inhalation exposure. International Journal of Toxicology 5(2):117-126.

**Health** Renal/Kidney

Outcome(s):

Reported Health

Relative kidney weight and renal tubular damage (histopathology)

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute- 4 hours **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 60771

Domain	Metric		Rating	Comments
Domain 5: Outcome Assessm	nent			
Me	etric 16:	Outcome Assessment Methodology	High	Outcome assessment and methodology were appropriate to measure outcome of interest.
Me	etric 17:	Consistency of Outcome Assessment	Medium	Details regarding outcomes assessment protocol were minimal, but unlikely to substantially impact results.
Me	etric 18:	Sampling Adequacy	High	The sampling was adequate. Renal pathology: n=4-5; Relative Kidney weight: n=5
Me	etric 19:	Blinding of Assessors	N/A	Blinding was not needed.
Me	etric 20:	Negative Control Response	Low	Negative control data was not reported for kidney histology.
Domain 6: Confounding / Va	ariable Con	ntrol		
Me	etric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant therefore respiratory rates should be reported.
Me	etric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.
Me	etric 23:	Data Presentation and Analysis	High	Statistical methods were described and appropriate.
Me	etric 24:	Reporting of Data	High	Data on exposure related outcomes were reported for kidney.

### **Overall Quality Determination**

### Medium

HERO ID: 60771 Table: 3 of 3

Study Citation: Francovitch, R.J., Schor, N.A., George, W.J. (1986). Effects of SKF 525A, phenobarbital, and 3-methylcholanthrene on ethylene dichloride toxicity

following inhalation exposure. International Journal of Toxicology 5(2):117-126.

Health

Hepatic/Liver

**Outcome(s):** 

**Reported Health** Relative liver weight

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- 4 hours **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 60771

Domain		Metric	Rating	Comments
Domain 1: Test Substan	nce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (1,2-dichloroethane).
	Metric 2:	Test Substance Source	Low	The source of the test substance was Aldrich Chemical Co., Milwaukee, Wisconsin. The batch/lot number were not provided.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported to be >99%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Appropriate negative control was included (air).
	Metric 5:	Positive Controls	N/A	A positive control was not required.
	Metric 6:	Randomized Allocation of Animals	Low	The authors do not report how the animals were allocated.
Domain 3: Exposure C	haracterization			
Bollain 3. Exposure C.	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not provided. Given the volatility of the test substance, this information would be useful.
	Metric 8:	Consistency of Exposure Administration	High	Test substance was administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Measured concentrations were not reported. The authors do report that they were within 10% of the theoretically generated concentration.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	One dose above the LOAEL was not included.
	Metric 12:	Exposure Route and Method	Medium	Exposure route and method (head-only) were appropriate and described in detail in sited reference (Franchovitch et al. 1985). However, the number of air changes/hour were not reported.
Domain 4: Test Animal	le.			
Domain 1. Test / Minne	Metric 13:	Test Animal Characteristics	Medium	Age and source of mice were not reported; however this is unlikely to have a substantial impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some husbandry conditions were reported (10 mice/cage, diet and water), all others were not reported.
	Metric 15:	Number of Animals per Group	Medium	The authors do not report exactly how many animals were treated/group. Figure 3 states that the 1500 ppm group contained 15 mice. Figures 1 and 2 report data from a minimum of 10 exposed mice from all dose group (except control). Table 1 (the only one with control reported) reports n=5. It can be concluded that n=5-15/ group, which is appropriate

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HERO ID: 60771 Table: 3 of 3

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Study Citation: Francovitch, R.J., Schor, N.A., George, W.J. (1986). Effects of SKF 525A, phenobarbital, and 3-methylcholanthrene on ethylene dichloride toxicity

following inhalation exposure. International Journal of Toxicology 5(2):117-126.

Health

Hepatic/Liver

Outcome(s):

**Reported Health** 

Relative liver weight

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute- 4 hours **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 60771

Domain		Metric	Rating	Comments
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment and methodology were appropriate to measure outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details on outcomes assessment protocols were minimal but unlikely to substantially impact results.
	Metric 18:	Sampling Adequacy	High	The sampling was adequate. Liver weight n=5/group.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not needed.
	Metric 20:	Negative Control Response	Low	Liver histology of negative control group was not reported.
Domain 6: Confoundir	ng / Variable Con	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant and therefore respiratory rates should be reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described and appropriate.
	Metric 24:	Reporting of Data	Medium	Data on liver histopathology is not reported. Authors state in that pathological changes were observed in exposed mice but do not provide incidence/severity or at which dose changes were seen.

## Overall Quality Determination Medium

HERO ID: 200352 Table: 1 of 1

Study Citation: Guo, X.L., Niu, Q. (2003). [The relationship between excitatory amino acids and acute intoxicated encephalopathy induced by 1,2-dichloroethane].

Zhonghua Laodong Weisheng Zhiyebing Zazhi / Chinese Journal of Industrial Hygiene and Occupational Diseases 21(2):83-85.

Health

Neurological/Behavioral

**Outcome(s):** 

**Reported Health** 

Water content of cortex and medulla; brain neurotransmitter levels

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single 12 hour exposure

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	Test substance identified as 1,2-dichloroethane
	Metric 2:	Test Substance Source	Low	Source identified as No. 1 Chemical Reagent Factory of Tianjin; batch/lot number not reported. Test substance identity was not analytically verified.
	Metric 3:	Test Substance Purity	Low	Purity was not reported
Domain 2: Test Design				
20 1000 2 001g.1	Metric 4:	Negative and Vehicle Controls	Low	Concurrent control group was reported but it is unclear if it was untreated or sham- treated.
	Metric 5:	Positive Controls	N/A	Not required for study type
	Metric 6:	Randomized Allocation of Animals	Medium	Study authors state that "rats were randomly divided into seven groups"
Domain 3: Exposure Ch	naracterization			
20mm 01 2mpoom 0	Metric 7:	Preparation and Storage of Test Substance	Low	Method of vapor generation was not reported other than "static total enclosure chamber" cited to Niu et al. 2002 (Hygiene Research 31:340), which is not available in HERO. No storage information was presented.
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported (no information on chamber designs, animals/chamber, etc.)
	Metric 9:	Reporting of Doses/Concentrations	Low	Nominal exposure concentrations were reported. Analytical concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	Medium	12 hour per day exposure; unclear whether this duration is appropriate to the endpoint
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	3 exposure concentrations (plus control) with 2x intervals were used. Effects seen at all concentrations so it is not clear that the low concentration was low enough.
	Metric 12:	Exposure Route and Method	Uninformative	Animals were exposed in a "static total enclosure chamber"
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and starting body weight were reported. Age was not reported. Source reported as Animal Experiment Center of Shanxi Medical University.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported to evaluate if husbandry was adequate and whether differences occurred between control and exposed populations. No information on temperature, relative humidity, light-dark cycle, or feed or water were reported.
	Metric 15:	Number of Animals per Group	Medium	6 animals per group were exposed. This number of exposed animals was sufficient for statistical analysis and is acceptable for an acute duration study.

Study Citation: Guo, X.L., Niu, Q. (2003). [The relationship between excitatory amino acids and acute intoxicated encephalopathy induced by 1,2-dichloroethane].

Zhonghua Laodong Weisheng Zhiyebing Zazhi / Chinese Journal of Industrial Hygiene and Occupational Diseases 21(2):83-85.

Health Neurological/Behavioral

**Outcome(s):** 

Reported Health

Water content of cortex and medulla; brain neurotransmitter levels

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Single 12 hour exposure

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200352

Domain		Metric	Rating	Comments
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Methods for measuring brain water content and for preparing brain tissue for analysis were reported; amino acid neurotransmitters analyzed by HPLC. It is not clear that these are sensitive indicators of neurological effects.
	Metric 17:	Consistency of Outcome Assessment	High	All animals were sacrificed for brain tissue sampling at the end of exposure except separate groups exposed to 10 mg/m3 and sacrificed after 2, 4, or 6 hr.
	Metric 18:	Sampling Adequacy	High	All animals were evaluated for the endpoint. Mass of brain tissue used to analyze neuro- transmitters was reported.
	Metric 19:	Blinding of Assessors	N/A	Not required for study type.
	Metric 20:	Negative Control Response	High	Control responses were reported and appeared normal.
Domain 6: Confoun	nding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Respiratory rate was not reported and 1,2-dichloroethane is expected to be a respiratory irritant
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis by one factor "variance analysis." Sufficient data were provided to conduct an independent statistical analysis.
	Metric 24:	Reporting of Data	High	Data for all endpoints reported with mean, SD, and n/group.

### **Overall Quality Determination**

### Uninformative

HERO ID: 4528351 Table: 1 of 8

Study Citation: Health	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane. Neurological/Behavioral; Gastrointestinal; Musculoskeletal;							
Outcome(s):								
Reported Health	Neurologica	Neurological/Behavioral: Clinical signs; Gastrointestinal: Diarrhea, necropsy findings; Musculoskeletal: Muscle weakness;						
Effect(s):	C	<b>C</b> ,						
Duration:	Acute (less t	han or equal to 24 hr) Oral - single dose						
Chemical:	1,1-Dichloro	oethane- Isomer: 1,2-Dichloroethane						
HERO ID:	4528351							
Domain		Metric	Rating	Comments				
Domain 1: Test Substan								
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified by a common chemical name.				
	Metric 2:	Test Substance Source	High	All Outcomes: Eastman Kodak was identified as the manufacturer.				
	Metric 3:	Test Substance Purity	Low	All Outcomes: Purity was not reported. The compound was freshly re-distilled; however, the methodology and resulting purity were not indicated.				
Domain 2: Test Design								
	Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: Acute lethality studies do not require a negative control.				
	Metric 5:	Positive Controls	N/A	All Outcomes: Acute lethality studies do not require a positive control.				
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.				
Domain 3: Exposure Ch	aracterization							
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile)				
	Metric 8:	Consistency of Exposure	Low	All Outcomes: No information is provided on gavage volume.				
		Administration						
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were provided as g/kg body weight.				
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Single oral dose is adequate for the study design.				
	Metric 11:	Number of Exposure Groups and	High	All Outcomes: 5 doses and the spacing was adequate to detect a range of responses.				
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	All Outcomes: The route and method were adequate for the study design.				
			<del>-</del>					
Domain 4: Test Animals			-					
	Metric 13:	Test Animal Characteristics	Low	All Outcomes: The source, strain, sex, age, and starting body weight were not reported.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not reported.				
	Metric 15:	Number of Animals per Group	Uninformative	All Outcomes: Only 1 animal/dose was used.				
Domain 5: Outcome Ass	sessment							
		Con	ntinued on next page .	••				

Blinding of Assessors

Negative Control Response

HERO ID: 4528351 Table: 1 of 8

All Outcomes: Blinding was not reported and assessment of clinical signs may be af-

for exposure-related findings were not shown for each study group, but results were

fected by knowledge of dose group.

described in the text.

All Outcomes: Negative controls were not used.

		cont	inued from previou	is page				
Study Citation: Health Outcome(s):	_	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane. Neurological/Behavioral; Gastrointestinal; Musculoskeletal;						
Reported Health Effect(s):	Neurologica	Neurological/Behavioral: Clinical signs; Gastrointestinal: Diarrhea, necropsy findings; Musculoskeletal: Muscle weakness;						
Duration: Chemical: HERO ID:		than or equal to 24 hr) Oral - single dose pethane- Isomer: 1,2-Dichloroethane						
Domain		Metric	Rating	Comments				
	Metric 16:	Outcome Assessment Methodology	Low	Neurological/Behavioral: The outcome assessment included an evaluation of clinical signs only. It was not clear if neurological tissues were examined by necropsy.; Gastrointestinal: The outcome assessment included an evaluation of clinical signs (i.d., diarrhea) and necropsy findings relate to gastric mucosa (methods not described).; Musculoskeletal: The outcome assessment included an evaluation of clinical signs only (i.e., muscle weakness). It was not clear if musculoskeletal tissues were examined by necropsy.				
	Metric 17:	Consistency of Outcome Assessment	Low	Neurological/Behavioral: Outcome assessment details were limited (e.g., timing of clinical observations).; Gastrointestinal: Outcome assessment details were limited (e.g., timing of clinical signs).; Musculoskeletal: Outcome assessment details were limited (e.g., timing of clinical observations).				
	Metric 18:	Sampling Adequacy	Low	Neurological/Behavioral: Details regarding sampling were not reported (i.e., how often were animals examined for clinical signs).; Gastrointestinal: Details regarding sampling were not reported (i.e., how often were animals examined for clinical signs, were all animals necropsied?).; Musculoskeletal: Details regarding sampling were not reported (i.e., how often were animals examined for clinical signs).				

Low

N/A

Metric 19:

Metric 20:

g / variable Con	11101		
Metric 21:	Confounding Variables in Test Design	Low	All Outcomes: Body weight change and food/water intake were not reported.
Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not possible (1 rabbit/group)
Metric 24:	Reporting of Data	Low	Neurological/Behavioral: Clinical signs were described in text only.; Gastrointestinal: Clinical signs and necropsy results were described in text only.; Musculoskeletal: Data

### **Overall Quality Determination**

### Uninformative

HERO ID: 4528351 Table: 2 of 8

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane. Ocular/Sensory; Cardiovascular; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Health Outcome(s): Reported Health Ocular/Sensory: Corneal effects; Cardiovascular: Necropsy findings; Nutritional/Metabolic: Decreased body weight; Hepatic/Liver: Necropsy findings; Renal/Kidney: Necropsy findings; Lung/Respiratory: Respiratory rate, necropsy findings; Effect(s): **Duration:** Acute (less than or equal to 24 hr) Oral - single dose Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 4528351 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: The test substance was identified by a common chemical name. Metric 2: Test Substance Source High All Outcomes: Eastman Kodak was identified as the manufacturer. Metric 3: **Test Substance Purity** Low All Outcomes: Purity was not reported. The compound was freshly re-distilled; however, the methodology and resulting purity were not indicated. Domain 2: Test Design Metric 4: Negative and Vehicle Controls N/A All Outcomes: Acute lethality studies do not require a negative control. Metric 5: Positive Controls N/A All Outcomes: Acute lethality studies do not require a positive control. Randomized Allocation of Animals Metric 6: Low All Outcomes: The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low All Outcomes: Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile) Substance Metric 8: Consistency of Exposure Low All Outcomes: No information is provided on gavage volume. Administration Reporting of Doses/Concentrations Metric 9: High All Outcomes: Doses were provided as g/kg body weight. **Exposure Frequency and Duration** High Metric 10: All Outcomes: Single oral dose is adequate for the study design. Number of Exposure Groups and Metric 11: High All Outcomes: 5 doses and the spacing was adequate to detect a range of responses. Dose/Concentration Spacing Metric 12: Exposure Route and Method High All Outcomes: The route and method were adequate for the study design. Domain 4: Test Animals Metric 13: Test Animal Characteristics Low All Outcomes: The source, strain, sex, age, and starting body weight were not reported. Metric 14: Adequacy and Consistency of Animal Low All Outcomes: Husbandry conditions were not reported. **Husbandry Conditions** Number of Animals per Group Metric 15: Uninformative All Outcomes: Only 1 animal/dose was used. Domain 5: Outcome Assessment

Continued on next page ...

#### Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane. **Study Citation:** 

Health Ocular/Sensory; Cardiovascular; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Lung/Respiratory;

**Outcome(s): Reported Health** Ocular/Sensory: Corneal effects; Cardiovascular: Necropsy findings; Nutritional/Metabolic: Decreased body weight; Hepatic/Liver: Necropsy findings;

Effect(s): Renal/Kidney: Necropsy findings; Lung/Respiratory: Respiratory rate, necropsy findings;

**Duration:** Acute (less than or equal to 24 hr) Oral - single dose Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Low	Ocular/Sensory: Necropsy findings were reported as clouding of the cornea (not furthed described) and methods were not described.; Cardiovascular: Necropsy findings were reported as heart (damage to specialized cells) and vascular damage (not further described) and methods were not described.; Nutritional/Metabolic: Loss of body weigh was reported for 1 rabbit at 600 mg/kg. Quantitative data were not provided.; Hepatic/Liver: Necropsy findings were reported as damage to specialized cells of the liver (not further described) and methods were not described.; Renal/Kidney: Necropsy findings were reported as damage to specialized cells of the kidney (not further described) and methods were not described of the kidney (not further described) and methods were not described.; Lung/Respiratory: Necropsy findings were reported as pulmonary edema, methods were not described. Decreased respiratory rate was also noted.
	Metric 17:	Consistency of Outcome Assessment	Low	Ocular/Sensory: Outcome assessment details were limited and it was not clear whether necropsy was conducted at a consistent timepoint.; Cardiovascular: Outcome assessment details were limited and it was not clear whether necropsy was conducted at a consistent timepoint.; Nutritional/Metabolic: Outcome assessment details were limited and it was not clear whether body weights were measured at a consistent timepoint.; Hepatic/Liver: Outcome assessment details were limited and it was not clear whether necropsy was conducted at a consistent timepoint.; Renal/Kidney: Outcome assessment details were limited and it was not clear whether necropsy was conducted at a consistent timepoint.; Lung/Respiratory: Outcome assessment details were limited and it was not clear whether necropsy was conducted at a consistent timepoint.
	Metric 18:	Sampling Adequacy	Low	Ocular/Sensory: Details regarding sampling were not reported (i.e., were all animals necropsied?).; Cardiovascular: Details regarding sampling were not reported (i.e., we all animals necropsied?).; Nutritional/Metabolic: Details regarding sampling were no reported (i.e., was body weight measured for all animals?).; Hepatic/Liver: Details re garding sampling were not reported (i.e., were all animals necropsied?).; Renal/Kidne Details regarding sampling were not reported (i.e., it was unclear if all animals were necropsied).; Lung/Respiratory: Details regarding sampling were not reported (i.e., it was unclear if all animals were necropsied).
	Metric 19:	Blinding of Assessors	N/A	Ocular/Sensory: Blinding is not necessary for this outcome.; Cardiovascular: Blindin is not necessary for this outcome.; Nutritional/Metabolic: Blinding is not necessary for this outcome.; Hepatic/Liver: Blinding is not necessary for this outcome.; Renal/Kidr Blinding is not necessary for this outcome; Lung/Respiratory: Blinding is not necessary for this outcome
	Metric 20:	Negative Control Response	N/A	All Outcomes: Negative controls were not used.

Domain 6: Confounding / Variable Control

Continued on next page ...

HERO ID: 4528351 Table: 2 of 8

1,1-Dichloroethane

#### ... continued from previous page

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health Ocular/Sensory; Cardiovascular; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Lung/Respiratory;

**Outcome(s):** 

Reported Health Ocular/Sensory: Corneal effects; Cardiovascular: Necropsy findings; Nutritional/Metabolic: Decreased body weight; Hepatic/Liver: Necropsy findings;

**Effect(s):** Renal/Kidney: Necropsy findings; Lung/Respiratory: Respiratory rate, necropsy findings;

**Duration:** Acute (less than or equal to 24 hr) Oral - single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Ocular/Sensory: Body weight change was incompletely reported and food/water intake were not reported.; Cardiovascular: Body weight change and food/water intake were not reported.; Nutritional/Metabolic: Body weight change and food/water intake were not reported.; Hepatic/Liver: Body weight change and food/water intake were not reported.; Renal/Kidney: Body weight change and food/water intake were not reported.; Lung/Respiratory: Body weight change and food/water intake were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not possible (1 rabbit/group)
	Metric 24:	Reporting of Data	Low	Ocular/Sensory: Necropsy results were described in text only.; Cardiovascular: Necropsy results were described in text only.; Nutritional/Metabolic: Body weight results were described in text only.; Hepatic/Liver: Necropsy results were described in text only.; Renal/Kidney: Data for exposure-related findings were not shown for each study group, but results were described in the text.; Lung/Respiratory: Data for exposure-related findings were not shown for each study group, but results were described in the text.

### **Overall Quality Determination**

### Uninformative

HERO ID: 4528351 Table: 3 of 8

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Nutritional/Metabolic

**Outcome(s):** Reported Health

Decreased body weight

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	·	Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	High	Eastman Kodak was identified as the manufacturer.
	Metric 3:	Test Substance Purity	Low	Purity was not reported. The compound was freshly re-distilled; however, the methodology and resulting purity were not indicated.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	Acute lethality studies do not require a negative control.
	Metric 5:	Positive Controls	N/A	Acute lethality studies do not require a positive control.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Cl	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile). Most of the test substance evaporated from the skin.
	Metric 8:	Consistency of Exposure Administration	Uninformative	The number of dermal applications differed across dose groups. Substance was applied in 5 ml volumes every 5 minutes until the desired amount was achieved.
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	Doses were not provided, because Table 3 was missing from the study pdf.
	Metric 10:	Exposure Frequency and Duration	High	Single day dosing was adequate for acute effects.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The number of dose groups was not provided, because Table 3 was missing from the study pdf.
	Metric 12:	Exposure Route and Method	High	The route and method were adequate for the study design.
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Low	4 animals/group.
Domain 5: Outcome As	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	Body weight was measured.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcome assessment details were limited (e.g., timing of body weight measurements).
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling were not reported (i.e., how often were bodyweight measurements performed).
	Metric 19:	Blinding of Assessors	N/A	Blinding not necessary for outcomes that are not subjective.
		Negative Control Response	N/A	- · ·

HERO ID: 4528351 Table: 3 of 8

#### ... continued from previous page

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Decreased body weight

Effect(s): Duration:

Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments			
Domain 6: Confounding / Variable Control							
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Food/water intake was not reported. A limited description of body weight changes were qualitatively described in the text.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed, because no controls were used.			
	Metric 24:	Reporting of Data	Uninformative	The report does not differentiate among findings in multiple exposure groups.			

### **Overall Quality Determination**

### Uninformative

HERO ID: 4528351 Table: 4 of 8

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Mortality

**Outcome(s):** 

Reported Health

Deaths

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	High	Eastman Kodak was identified as the manufacturer.
	Metric 3:	Test Substance Purity	Low	Purity was not reported. The compound was freshly re-distilled; however, the methodology and resulting purity were not indicated.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	Acute lethality studies do not require a negative control.
	Metric 5:	Positive Controls	N/A	Acute lethality studies do not require a positive control.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile). Most of the test substance evaporated from the skin.
	Metric 8:	Consistency of Exposure Administration	Uninformative	The number of dermal applications differed across dose groups. Substance was applied in 5 ml volumes every 5 minutes until the desired amount was achieved.
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	Doses were not provided, because Table 3 was missing from the study pdf.
	Metric 10:	Exposure Frequency and Duration	High	Single day dosing was adequate for acute effects.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The number of dose groups was not provided, because Table 3 was missing from the study pdf.
	Metric 12:	Exposure Route and Method	High	The route and method were adequate for the study design.
Domain 4: Test Animals	s			
	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Low	4 animals/group.
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment included an evaluation of clinical signs only (i.e., death). Necropsy was not performed.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding not necessary for outcome.
		Con	ntinued on next page .	

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 4528351 Table: 4 of 8

#### ... continued from previous page

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Mortality

**Outcome(s):** 

Reported Health

Deaths

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	N/A	Negative controls were not used.
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not possible, because quantitative data were not provided.
	Metric 24:	Reporting of Data	Low	Mortality data was described in text only; data were not provided for each dose group.

### **Overall Quality Determination**

### Uninformative

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Irritation

**Outcome(s):** 

Reported Health

Gastrointestinal (oral), skin (dermal)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID: 4:	528351			
Domain		Metric	Rating	Comments
Domain 1: Test Substance				
N	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	High	Eastman Kodak was identified as the manufacturer.
N	Metric 3:	Test Substance Purity	Low	Purity was not reported. The compound was freshly re-distilled; however, the methodology and resulting purity were not indicated.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	Acute lethality studies do not require a negative control.
$\mathbf{N}$	Metric 5:	Positive Controls	N/A	Acute lethality studies do not require a positive control.
N	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Charac	cterization			
-	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile). Most of the test substance evaporated from the skin.
N	Metric 8:	Consistency of Exposure Administration	Uninformative	The number of dermal applications differed across dose groups. Substance was applied in 5 ml volumes every 5 minutes until the desired amount was achieved.
N	Metric 9:	Reporting of Doses/Concentrations	Uninformative	Doses were not provided, because Table 3 was missing from the study pdf.
N	Metric 10:	Exposure Frequency and Duration	High	Single day dosing was adequate for acute effects.
N	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The number of dose groups was not provided, because Table 3 was missing from the study pdf.
N	Metric 12:	Exposure Route and Method	High	The route and method were adequate for the study design.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
M	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
N	Metric 15:	Number of Animals per Group	Low	4 animals/group.
Domain 5: Outcome Assess	sment			
	Metric 16:	Outcome Assessment Methodology	Low	Study authors state that "in no case did local damage result." However, the outcome assessment methodology was not described.
N	Metric 17:	Consistency of Outcome Assessment	Low	Outcome assessment details were not provided (i.e., timing/frequency skin was examined for evidence of irritation).
N	Metric 18:	Sampling Adequacy	Low	Details regarding sampling were not reported.
		Con	ntinued on next page	

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane. **Study Citation:** Irritation

Health

**Outcome(s):** Reported Health

Gastrointestinal (oral), skin (dermal)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	Low	Blinding was not reported and assessment of skin irritation may be affected by knowledge of dose group.
	Metric 20:	Negative Control Response	N/A	Negative controls were not used.
Domain 6: Confound	ling / Variable Co			
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Body weight change and food/water intake were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not possible, because quantitative data were not provided.
	Metric 24:	Reporting of Data	High	Clearly negative findings were reported qualitatively in the text.

### **Overall Quality Determination**

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Lung/Respiratory

**Outcome(s):** 

Reported Health

Respiratory rate, necropsy findings

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	High	Eastman Kodak was identified as the manufacturer.
	Metric 3:	Test Substance Purity	Low	Purity was not reported. The compound was freshly re-distilled; however, the methodology and resulting purity were not indicated.
Domain 2: Test Design	l			
	Metric 4:	Negative and Vehicle Controls	N/A	Acute lethality studies do not require a negative control.
	Metric 5:	Positive Controls	N/A	Acute lethality studies do not require a positive control.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile). Most of the test substance evaporated from the skin.
	Metric 8:	Consistency of Exposure Administration	Uninformative	The number of dermal applications differed across dose groups. Substance was applied in 5 ml volumes every 5 minutes until the desired amount was achieved.
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	Doses were not provided, because Table 3 was missing from the study pdf.
	Metric 10:	Exposure Frequency and Duration	High	Single day dosing was adequate for acute effects.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The number of dose groups was not provided, because Table 3 was missing from the study pdf.
	Metric 12:	Exposure Route and Method	High	The route and method were adequate for the study design.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Low	4 animals/group.
Domain 5: Outcome A	ssessment			
2. Outomo 11	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment included an evaluation of clinical signs only (i.e., increased respiratory rate). Necropsy was not performed.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcome assessment details were limited (e.g., timing of clinical signs).
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling were not reported (i.e., how often were animals examined for clinical signs).
		Col	ntinued on next page .	

HERO ID: 4528351 Table: 6 of 8

#### ... continued from previous page

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Lung/Respiratory

**Outcome(s):** 

Reported Health

Effect(s):

Respiratory rate, necropsy findings

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	Low	Blinding was not reported and assessment of clinical signs may be affected by knowledge of dose group.
	Metric 20:	Negative Control Response	N/A	Negative controls were not used.
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not possible, because quantitative data were not provided.
	Metric 24:	Reporting of Data	Uninformative	The report does not differentiate among findings in multiple exposure groups.

### **Overall Quality Determination**

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 4528351 Table: 7 of 8

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Gastrointestinal

**Outcome(s):** 

Reported Health

Diarrhea, necropsy findings

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	High	Eastman Kodak was identified as the manufacturer.
	Metric 3:	Test Substance Purity	Low	Purity was not reported. The compound was freshly re-distilled; however, the methodology and resulting purity were not indicated.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	Acute lethality studies do not require a negative control.
	Metric 5:	Positive Controls	N/A	Acute lethality studies do not require a positive control.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	aracterization			
·	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile). Most of the test substance evaporated from the skin.
	Metric 8:	Consistency of Exposure Administration	Uninformative	The number of dermal applications differed across dose groups. Substance was applied in 5 ml volumes every 5 minutes until the desired amount was achieved.
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	Doses were not provided, because Table 3 was missing from the study pdf.
	Metric 10:	Exposure Frequency and Duration	High	Single day dosing was adequate for acute effects.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The number of dose groups was not provided, because Table 3 was missing from the study pdf.
	Metric 12:	Exposure Route and Method	High	The route and method were adequate for the study design.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Low	4 animals/group.
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment included an evaluation of clinical signs only (i.e., diarrhea). Necropsy was not performed.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcome assessment details were limited (e.g., timing of clinical signs).
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling were not reported (i.e., how often were animals examined for clinical signs).
	Metric 19:	Blinding of Assessors	N/A	Not applicable for outcomes that are not subjective.
		Con	ntinued on next page .	

HERO ID: 4528351 Table: 7 of 8

#### ... continued from previous page

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Gastrointestinal

**Outcome(s):** 

Reported Health

Diarrhea, necropsy findings

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Dermal - single day (single or multiple applications)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	N/A	Negative controls were not used.
Domain 6: Confoun	nding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that the state of th
	Metric 23: Metric 24:	Data Presentation and Analysis Reporting of Data	N/A Low	tion) that could influence the outcome assessment.  Statistical analysis was not possible, because quantitative data were not provided.  Clinical signs were described in text only; data were not provided for each dose group.

### **Overall Quality Determination**

HERO ID: 4528351 Table: 8 of 8

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Mortality

**Outcome(s):** 

Reported Health

Deaths

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Oral - single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	Low	The source was not identified.
	Metric 3:	Test Substance Purity	Low	Purity was not reported.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	N/A	Negative controls not required for acute study design.
	Metric 5:	Positive Controls	N/A	Positive control not required for acute study design.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	aracterization			
1	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile)
	Metric 8:	Consistency of Exposure	Low	No information is provided on gavage volume.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were provided as g/kg body weight.
	Metric 10:	Exposure Frequency and Duration	High	Single oral dose is adequate for the study design.
	Metric 11:	Number of Exposure Groups and	High	5 doses and the spacing was adequate to detect a range of responses.
	Metric 11.	Dose/Concentration Spacing	High	3 doses and the spacing was adequate to detect a range of responses.
	Metric 12:	Exposure Route and Method	High	The route and method were adequate for the study design.
Domain 4: Test Animals	2			
Domain 4. Test / minus	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Uninformative	Only 1 animals/group was used.
Domain 5: Outcome Ass	sessment			
Domain J. Outcome Ass	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details were not reported, but daily examination for mortality are likely.
	Metric 18:	Sampling Adequacy	High	Each animals was examined for death.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	N/A N/A	Negative controls were not used.
	1vicuic 20.	regative Control Response	11///	regauve controls were not used.

Domain 6: Confounding / Variable Control

Continued on next page ...

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 4528351 Table: 8 of 8

#### ... continued from previous page

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Mortality

**Outcome(s):** 

Reported Health Deaths

Effect(s): **Duration:** 

Chemical:

Acute (less than or equal to 24 hr) Oral - single dose 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not possible (1 rabbit/group)
	Metric 24:	Reporting of Data	High	Mortality data were provided for each group/animal.

### **Overall Quality Determination**

Study Citation:	Kitchin, K.T	Г., Brown, J.L., Kulkarni, A.P. (1993). Predic	ting rodent	carcinogenicity of halogenated hydrocarbons by in vivo biochemical parameters. Birth
•	Defects Res	earch, Part B: Developmental and Reproduc	-	
Health	Hepatic/Live	er; Genotox (Genotox); Mortality;		
Outcome(s):				
Reported Health			ecarboxylas	e activity and cytochrome P-450 content; Genotox (Genotox): Hepatic DNA damage
Effect(s):	. •	elution); Mortality: Mortality.;		
Duration:		than or equal to 24 hr) 21 hours		
Chemical:	*	bethane- Isomer: 1,2-Dichloroethane		
HERO ID:	6118			
Domain		Metric	Rating	Comments
Domain 1: Test Substan		The Color of the Co	TT' 1	
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was not identified.
	Metric 3:	Test Substance Purity	Low	All Outcomes: The purity of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Appropriate negative controls were included.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control was not required.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The authors do not report how the animals were allocated.
				•
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test	Low	All Outcomes: Preparation and storage conditions were not provided. Given the volatil-
		Substance		ity of the test substance, this information would be useful.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Test substance was administered consistently across study groups
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Doses are reported in Table I without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency was provided without ambiguity (21 and 4 hours
	Metric 10.	Exposure Prequency and Duration	High	before sacrifice).
	Metric 11:	Number of Exposure Groups and	Low	All Outcomes: Only one dose was studied. This dose was chosen based on either LD50
		Dose/Concentration Spacing		or cancer bioassays. No effect on apical outcome was seen.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route of exposure was gavage and was appropriate.
Domain 4: Test Animal	c			
Domain T. 10st / Illillian	Metric 13:	Test Animal Characteristics	High	All Outcomes: All relevant animal characteristics were reported.
	Metric 13:	Adequacy and Consistency of Animal	Medium	All Outcomes: Rats were caged 3 per cage and provided food and water ad libitum.
	Metric 14.	Husbandry Conditions	Wicdiani	Other husbandry conditions were not reported but this is unlikely to substantially impact results.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was appropriate.
D : 50: .				
Domain 5: Outcome As		Outrous Assessment Method 1	TT: _L	All O
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology was appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: The sampling was adequate.
		Contin	nued on nex	xt page

		···contin	ueu mom p	revious page		
<b>Study Citation:</b>		Kitchin, K.T., Brown, J.L., Kulkarni, A.P. (1993). Predicting rodent carcinogenicity of halogenated hydrocarbons by in vivo biochemical parameters. Birth Defects Research, Part B: Developmental and Reproductive Toxicology 13(4):167-184.				
Health		er; Genotox (Genotox); Mortality;	tive Toxicoi	ogy 13(+).107-104.		
Outcome(s):						
Reported Health	Henatic/Live	er: Serum ALT activity, henatic ornithine de	ecarboxylas	e activity and cytochrome P-450 content; Genotox (Genotox): Hepatic DNA damage		
Effect(s):		elution); Mortality: Mortality.;				
Duration:		han or equal to 24 hr) 21 hours				
Chemical:	,	bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	6118					
	0110					
Domain		Metric	Rating	Comments		
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary.		
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were appropriate.		
Domain 6: Confound	ng / Variable Co	ntrol				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.		
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were described and appropriate.		
	Metric 24:	Reporting of Data	High	All Outcomes: All data were reported.		
			High	•		
Overall Qual	Overall Quality Determination					

Study Citation: Kronevi, T., Wahlberg, J.E., Holmberg, B. (1981). Skin pathology following epicutaneous exposure to seven organic solvents. International Journal of

Tissue Reactions 3(1):21-30.

**Health** Skin/Connective Tissue

**Outcome(s):** 

**Reported Health** Localized microscopic examinations of the skin (at the application site)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 15 minutes, and 1, 4, and 16 hours

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was clearly identified using standard nomenclature. A CASRN was not provided.
	Metric 2:	Test Substance Source	Low	The test substance source was reported, but a lot and batch number were not provided and the substance identity was not analytically verified.
	Metric 3:	Test Substance Purity	Low	The test substance purity was not reported. It was specified to be "certified, inhibited"
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	Adjacent un-exposed skin served as the negative control.
	Metric 5:	Positive Controls	N/A	A positive control was not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	N/A	There was only one group, randomization was not necessary
Domain 3: Exposure Ch	aracterization			
Domain or Emposare on	Metric 7:	Preparation and Storage of Test Substance	Medium	The test substance was applied undiluted; no preparation was necessary. It was not spec ified how the undiluted samples were stored. This is not expected to have a significant impact on the study results.
	Metric 8:	Consistency of Exposure Administration	High	The exposure details were clearly described. Consistency is NA because there was only one study group.
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	A dose (in mg/kg) was not specified but the volume applied and a range of animal body weights was provided which could allow a rough estimate of the dose. However, due to insufficient study details, there is significant ambiguity because it is unknown whether multiple exposure chambers were applied to a single animal.
	Metric 10:	Exposure Frequency and Duration	High	The exposure times selected allowed the demonstration of an increase in the severity of effects with exposure time, and appeared to be appropriate for the purposes of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	This study altered the time of exposure instead of testing multiple doses. There was only one exposure concentration.
	Metric 12:	Exposure Route and Method	High	The route of exposure (dermal) was appropriate for the purposes of the study, and the study authors took measures to mitigate possible exposure via other routes (e.g., inhalation or oral)
Domain 4: Test Animals				
Domain 4. 16st Amilian	Metric 13:	Test Animal Characteristics	Low	The species, sex, and a range of body weights were provided. No further animal details were provided (e.g., strain, age, and source).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not reported.

<b>Study Citation:</b>	Kronevi, T., Wahlberg, J.E., Holmberg, B. (1981). Skin pathology following epicutaneous exposure to seven organic solvents. International Journal of
	Tissue Reactions 3(1):21-30.

Health

Skin/Connective Tissue

**Outcome(s):** 

**Reported Health** 

Localized microscopic examinations of the skin (at the application site)

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) 15 minutes, and 1, 4, and 16 hours

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 58151

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	The number of animals used was not reported. The study indicates that 17 animals were included and the study tested 7 different chemicals. It is likely only 1 or 2 animals were tested for each chemical; although, this is not specified. It was not clearly indicated if the same animals had multiple application sites (one for each timepoint).
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	The purposes of the study were not clearly reported; the study examined histopathological changes to the skin at the administration site, which is considered to be a sensitive method for identifying damage to the skin. The number of slides examined was not specified.
	Metric 17:	Consistency of Outcome Assessment	High	Consistency of outcome assessment is not applicable to this study because only a single exposure group was included; however, the same method was applied across time points.
	Metric 18:	Sampling Adequacy	Low	The study does not specify how many animals were exposed or how many slides from each site were examined.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	The study indicated that no lesions were observed at the un-exposed control sites.
Domain 6: Confoundi	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Possible confounding between groups was not an issue for this study because only a single group was tested.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Confounding among groups due to health outcomes is not applicable to this study.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not relevant (single exposure group)
	Metric 24:	Reporting of Data	High	A clear description of histopathological findings at each time point was provided with an indication of severity. The data tables do not indicate the number of animals the data were obtained from.

# **Overall Quality Determination**

Study Citation: Health	Livesey, J. C. (1982). Studies on the metabolism and toxicity of 1,2-dihaloethanes.  Renal/Kidney; Hepatic/Liver;					
Outcome(s):	· · · · · · · · · · · · · · · · · · ·					
Reported Health		Renal/Kidney: BUN, serum creatinine levelsUrine was collected and analyzed for LDH, alkaline phophatase, g-glutamyl transpeptidase, urine flow rate				
Effect(s):		ity; Hepatic/Liver: Serum ALT (GPT) levels	s;			
Duration:		than or equal to 24 hr) Acute				
Chemical:		bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	5540663					
Domain		Metric	Rating	Comments		
Domain 1: Test Substance						
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.		
	Metric 2:	Test Substance Source	Low	All Outcomes: The source the test substance was Aldrich Chemical Co, Milwaukee, WI. Lot/Batch number were not provided.		
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity of test substance was reported as 99+%, gold label.		
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A negative control group was appropriate.		
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.		
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Study does not report how animals were allocated.		
Domain 3: Exposure Ch	aracterization					
Domain of Emposare Cir	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Preparation and storage were not adequately described given the volatility of the test substance.		
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance was delivered consistently across study groups.		
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses studied were reported.		
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were reported and appropriate.		
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Number of dose groups was adequate for aim of this study.		
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route and method were appropriate.		
Domain 4: Test Animals	S					
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Test animal characteristics were adequately reported.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Not all husbandry conditions were reported, this is unlikely to have a substantial impact on results.		
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals/group were not clearly reported.		
Domain 5: Outcome Ass	recement					
Domain 5. Outcome Ass	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Histological analysis was not performed on organs.		
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The outcomes were assessed consistently across study groups.		
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Details regarding sampling of outcomes were not sufficiently reported.		
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.		
	Metric 20:	Negative Control Response	High	All Outcomes: A negative control group was adequate.		
	·					
Continued on next page						

HERO ID: 5540663 Table: 1 of 1

1,1-Dichloroethane

#### ... continued from previous page

**Study Citation:** Livesey, J. C. (1982). Studies on the metabolism and toxicity of 1,2-dihaloethanes.

Health

Renal/Kidney; Hepatic/Liver;

**Outcome(s):** 

Reported Health Renal/Kidney: BUN, serum creatinine levelsUrine was collected and analyzed for LDH, alkaline phophatase, g-glutamyl transpeptidase, urine flow rate

**Effect(s):** and osmolality; Hepatic/Liver: Serum ALT (GPT) levels;

**Duration:** Acute (less than or equal to 24 hr) Acute

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5540663

Domain		Metric	Rating	Comments
Domain 6: Confound	ling / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis were adequately reported.
	Metric 24:	Reporting of Data	Medium	All Outcomes: Minor uncertainties in reporting outcome data. Not all timepoints were reported (unclear if these timepoints were negative).

High

# Overall Quality Determination

**Study Citation:** 

Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health

Nutritional/Metabolic; Lung/Respiratory; Mortality; Hepatic/Liver;

Outcome(s):

Reported Health

Nutritional/Metabolic: Weight change; Lung/Respiratory: Gross pathology; Mortality: Death (LD50); Hepatic/Liver: Gross pathology;

Effect(s):

**Duration:**Acute (less than or equal to 24 hr) Acute-Inhalation**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447301

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ance			
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name and CASRN
	Metric 2:	Test Substance Source	High	All Outcomes: Source clearly reported; it is presumed to be a commercial source (S. Charleston), but the study is old (1945), and the source is not recognized as a known/common source. It appears as though batch no and lot or stock numbers were provided. The test substance was not analytically verified.
	Metric 3:	Test Substance Purity	Medium	All Outcomes: Reported as commercial grade. In the time-period of the study, it is uncertain what purity "commercial grade" represents.
Domain 2: Test Desig	n			
	Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: A negative control is not required for this study type.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for acute toxicity studies
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animal allocation was not report
Domain 3: Exposure (	Characterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Beyond indication of vehicles used for dilution no other information of test solution preparation or storage were provided.
	Metric 8:	Consistency of Exposure Administration	Low	Nutritional/Metabolic: Details of exposure administration were not provided.; Lung/Respiratory: Details of exposure administration were not provided. Animals used for different durations of exposure were not exposed on the same study days, therefore these were considered to be three separate experiments.; Mortality: Details of exposure administration were not provided.; Hepatic/Liver: Details of exposure administration were not provided. Animals used for different durations of exposure were not exposed on the same study days, therefore these were considered to be three separate experiments.
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Exposure concentrations were reported; it is not indicated that these were analytically verified.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type and/or outcome(s) of interest. 3 different exposure times were evaluated.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Study consisted of a single exposure group, but due to use of different exposure times, an appropriate effect was observed.
	Metric 12:	Exposure Route and Method	Uninformative	All Outcomes: There was no description of the inhalation chamber, or the methods of exposure.

Domain 4: Test Animals

HERO ID: 5447301 Table: 1 of 5

#### ... continued from previous page

Study Citation: Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health Nutritional/Metabolic; Lung/Respiratory; Mortality; Hepatic/Liver;

Outcome(s):

Reported Health Nutritional/Metabolic: Weight change; Lung/Respiratory: Gross pathology; Mortality: Death (LD50); Hepatic/Liver: Gross pathology;

Effect(s):

**Duration:**Acute (less than or equal to 24 hr) Acute-Inhalation**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447301

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Minimal details on test animals were provided species and sex only
	Metric 14:	Adequacy and Consistency of Animal	Low	All Outcomes: Husbandry conditions were not reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Medium	All Outcomes: The number of animals per dose group was adequate for the study type/outcome analysis.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: All animals were evaluated, and Animals were observed for up to 14 days.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Details of outcome assessment were not reported
	Metric 18:	Sampling Adequacy	High	All Outcomes: All animals were observed.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: not necessary for study type
	Metric 20:	Negative Control Response	N/A	All Outcomes: No control is required for this assay
Domain 6: Confoundi	ng / Variable Co	ntrol		
Domain o. Comounar	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: Although the study did not report all information to determine confound-
	Wettle 21.	and Procedures	Wedium	ing, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not necessary for this study type (control group not necessary)
	Metric 24:	Reporting of Data	High	Nutritional/Metabolic: Individual animal data were provided.; Lung/Respiratory: Individual animal data were provided.; Mortality: Mortality results were clearly reported, although no LC50 was indicated.; Hepatic/Liver: Individual animal data were provided.

### **Overall Quality Determination**

HERO ID: 5447301 Table: 2 of 5

1,1-Dichloroethane

**Study Citation:** 

Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health

Mortality

**Outcome(s):** 

Reported Health

Death (LD50)

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute-Oral Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447301

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Identified by name and CASRN
	Metric 2:	Test Substance Source	High	Source clearly reported; it is presumed to be a commercial source (S. Charleston), but the study is old (1945), and the source is not recognized as a known/common source. It appears as though batch no and lot or stock numbers were provided. The test substance was not analytically verified.
	Metric 3:	Test Substance Purity	Medium	Reported as commercial grade. In the time-period of the study, it is uncertain what purity "commercial grade" represents.
Domain 2: Test Desi	gn			
	Metric 4:	Negative and Vehicle Controls	N/A	A negative control is not required for this study type.
	Metric 5:	Positive Controls	N/A	Not necessary for acute toxicity studies
	Metric 6:	Randomized Allocation of Animals	Low	Animal allocation was not report
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Beyond indication of vehicles used for dilution no other information of test solution preparation or storage were provided.
	Metric 8:	Consistency of Exposure Administration	Uninformative	Animals both within the same group and between groups were dosed on different days (in some instances months apart). Administered volumes varied both within and between dose groups
	Metric 9:	Reporting of Doses/Concentrations	Medium	Doses were clearly reported. It is not indicated that these were analytical measurements.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and/or outcome(s) of interest
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Study included 4 dose groups (and presumably a vehicle control?)
	Metric 12:	Exposure Route and Method	High	The route (oral intubation) is suited to the test substance
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Low	Minimal details on test animals were provided species and sex only
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per dose group was adequate for the study type/outcome analysis.

#### Domain 5: Outcome Assessment

#### Continued on next page ...

HERO ID: 5447301 Table: 2 of 5

#### ... continued from previous page

Study Citation: Health Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Mortality

**Outcome(s):** 

Reported Health

Death (LD50)

Effect(s):
Duration:
Chemical:

Acute (less than or equal to 24 hr) Acute-Oral 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447301

Domain	Metric	Rating	Comments
Metric 16:	Outcome Assessment Methodology	High	Animals were observed for mortality; the duration of observation was not clearly reported, but was at least 5 days since the death of one animal was reported 5 days post-dosing.
Metric 17:	Consistency of Outcome Assessment	Low	Details of outcome assessment were not reported
Metric 18:	Sampling Adequacy	High	All animals were observed.
Metric 19:	Blinding of Assessors	N/A	not necessary for study type
Metric 20:	Negative Control Response	N/A	No control is required for this assay
Domain 6: Confounding / Variable Co	ontrol  Confounding Variables in Test Design	Medium	Although the study did not report all information to determine confounding, reported
Mettic 21.	and Procedures	Medium	information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not necessary for this study type (control group not necessary)
Metric 24:	Reporting of Data	High	Individual animal data were provided.

# **Overall Quality Determination**

HERO ID: 5447301 Table: 3 of 5

**Study Citation:** 

Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health

Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;

**Outcome(s):** 

Reported Health

Renal/Kidney: Gross Pathology; Hepatic/Liver: Gross pathology; Lung/Respiratory: Gross pathology; Gastrointestinal: Gross pathology;

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute-Oral **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID.	J <del>11</del> /J01			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name and CASRN
	Metric 2:	Test Substance Source	High	All Outcomes: Source clearly reported; it is presumed to be a commercial source (S. Charleston), but the study is old (1945), and the source is not recognized as a known/common source. It appears as though batch no and lot or stock numbers were provided. The test substance was not analytically verified.
	Metric 3:	Test Substance Purity	Medium	All Outcomes: Reported as commercial grade. In the time-period of the study, it is uncertain what purity "commercial grade" represents.
Domain 2: Test Design				
Č	Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: A negative control is not required for this study type.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for acute toxicity studies
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animal allocation was not report
Domain 3: Exposure C	haracterization			
1	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Beyond indication of vehicles used for dilution no other information of test solution preparation or storage were provided.
	Metric 8:	Consistency of Exposure Administration	Uninformative	Renal/Kidney: Animals both within the same group and between groups were dosed on different days (in some instances months apart). Gavage volumes varied both within and between dose groups; Hepatic/Liver: Gavage volumes varied both within and between dose groups; Animals both within the same group and between groups were dosed on different days (in some instances months apart).; Lung/Respiratory: Animals both within the same group and between groups were dosed on different days (in some instances months apart). Gavage volumes varied both within and between groups were dosed on different days (in some instances months apart). Gavage volumes varied both within and between dose groups
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Doses were clearly reported. It is not indicated that these were analytical measurements.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type and/or outcome(s) of interest
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Study included 4 dose groups (and presumably a vehicle control?)
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route (oral intubation) is suited to the test substance
Domain 4: Test Animal	ls			
2 cmain ii 10st I minus	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Minimal details on test animals were provided species and sex only
		Con	ntinued on next page .	

HERO ID: 5447301 Table: 3 of 5

#### ... continued from previous page

Study Citation: Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;

**Outcome(s):** 

Reported Health

Renal/Kidney: Gross Pathology; Hepatic/Liver: Gross pathology; Lung/Respiratory: Gross pathology; Gastrointestinal: Gross pathology;

**Effect(s):** 

**Duration:**Acute (less than or equal to 24 hr) Acute-Oral**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447301

Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal	Low	All Outcomes: Husbandry conditions were not reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Medium	All Outcomes: The number of animals per dose group was adequate for the study
				type/outcome analysis.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: Animals were observed for gross pathology; no further details of outcome assessment methodology were provided.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Details of outcome assessment were not reported
	Metric 18:	Sampling Adequacy	High	All Outcomes: All animals were observed.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: not necessary for study type
	Metric 20:	Negative Control Response	N/A	All Outcomes: No control is required for this assay
Domain 6: Confounding	og / Variable Co	ntral		
Domain o. Comountin	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: Although the study did not report all information to determine confound-
	Metric 21.	and Procedures	Wedium	ing, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not necessary for this study type (control group not necessary)
	Metric 24:	Reporting of Data	Low	All Outcomes: Some gross pathology findings were described in the text but did not differentiate between groups or provide incidences

### **Overall Quality Determination**

HERO ID: 5447301 Table: 4 of 5

**Study Citation:** 

Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health

Mortality

**Outcome(s):** 

Reported Health

Death (LD50)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute-Dermal **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	Identified by name and CASRN
	Metric 2:	Test Substance Source	High	Source clearly reported; it is presumed to be a commercial source (S. Charleston), but the study is old (1945), and the source is not recognized as a known/common source. It appears as though batch no and lot or stock numbers were provided. The test substance was not analytically verified.
	Metric 3:	Test Substance Purity	Medium	Reported as commercial grade. In the time-period of the study, it is uncertain what purity "commercial grade" represents.
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	N/A	A negative control is not required for this study type.
	Metric 5:	Positive Controls	N/A	Not necessary for acute toxicity studies
	Metric 6:	Randomized Allocation of Animals	Low	Animal allocation was not report
Domain 3: Exposure	Characterization			
Bollium 3. Exposure	Metric 7:	Preparation and Storage of Test	Low	Substance administered undiluted. Storage was not reported.
	Metric 8:	Substance Consistency of Exposure Administration	Uninformative	Animals both within the same group and between groups were dosed on different days (in some instances months apart). Administered volumes varied both within and between dose groups.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Doses were clearly reported. It is not indicated that these were analytical measurements.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and/or outcome(s) of interest
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Study included 4 dose groups
	Metric 12:	Exposure Route and Method	Medium	The route is suited to the test substance; the method is not described in detail, but a Vinylite Dam was used, which appears to be a tape that would provide an occluded condition to prevent evaporation. The volumes used appear to be excessive although the area covered was not reported.
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	Low	Minimal details on test animals were provided species and sex only
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per dose group was adequate for the study type/outcome analysis.

#### Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

**Study Citation:** 

Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

Death (LD50)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute-Dermal **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447301

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric	16: Outcome Assessment Methodology	High	Animals were observed for up to 14 days
Metric	17: Consistency of Outcome Assessment	Medium	Details of outcome assessment were not reported, but animals appeared to be consistently observed
Metric	18: Sampling Adequacy	High	All animals were observed.
Metric	19: Blinding of Assessors	N/A	not necessary for study type
Metric	20: Negative Control Response	N/A	No control is required for this assay
Domain 6: Confounding / Variable Metric	21: Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
Metric	22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric	23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary for this study type (control group not necessary), although the method used for LD50 determination was reported
Metric	24: Reporting of Data	High	Data for individual animals were reported

# **Overall Quality Determination**

HERO ID: 5447301 Table: 5 of 5

**Study Citation:** 

Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Weight change

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute-Dermal **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

544/301			
	Metric	Rating	Comments
ance			
Metric 1:	Test Substance Identity	High	Identified by name and CASRN
Metric 2:	Test Substance Source	High	Source clearly reported; it is presumed to be a commercial source (S. Charleston), but the study is old (1945), and the source is not recognized as a known/common source. It appears as though batch no and lot or stock numbers were provided. The test substance was not analytically verified.
Metric 3:	Test Substance Purity	Medium	Reported as commercial grade. In the time-period of the study, it is uncertain what purity "commercial grade" represents.
gn			
Metric 4:	Negative and Vehicle Controls	N/A	A negative control is not required for this study type.
Metric 5:	Positive Controls	N/A	Not necessary for acute toxicity studies
Metric 6:	Randomized Allocation of Animals	Low	Animal allocation was not report
Characterization			
Metric 7:	Preparation and Storage of Test	Low	Substance administered undiluted. Storage was not reported.
Metric 8:	Substance Consistency of Exposure Administration	Uninformative	Animals both within the same group and between groups were dosed on different days. Administered volumes varied both within and between dose groups
Metric 9:	Reporting of Doses/Concentrations	Medium	Doses were clearly reported. It is not indicated that these were analytical measurements.
Metric 10:	Exposure Frequency and Duration	Medium	24hr exposure; it was not indicated if patches were then removed or if skin was washed.
Metric 11:	Number of Exposure Groups and	High	Study included 4 dose groups
Metric 12:	Dose/Concentration Spacing Exposure Route and Method	Low	The route is suited to the test substance; the method is not described in detail, but a Vinylite Dam was used, which appears to be a tape that would provide an occluded condition to prevent evaporation. The volumes used appear to be excessive although the area covered was not reported.
als			
Metric 13:	Test Animal Characteristics	Low	Minimal details on test animals were provided species and sex only
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
Metric 15:	Number of Animals per Group	Medium	The number of animals per dose group was adequate for the study type/outcome analysis.
Assessment			
Metric 16:	Outcome Assessment Methodology	High	Body weights were measured on day 14 for surviving animals
	Coi	ntinued on next page .	•••
	Metric 1: Metric 2:  Metric 2:  Metric 3:  Metric 4: Metric 5: Metric 6:  Characterization Metric 7: Metric 8: Metric 9: Metric 10: Metric 11: Metric 12:  Matric 12:  Metric 13: Metric 14: Metric 15:	Metric 1: Test Substance Identity Metric 2: Test Substance Source  Metric 3: Test Substance Purity  Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Characterization Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  mals Metric 13: Test Animal Characteristics Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Metric 15: Number of Animals per Group  Assessment Metric 16: Outcome Assessment Methodology	Metric 1: Test Substance Identity High Metric 2: Test Substance Source High  Metric 3: Test Substance Purity Medium  Metric 3: Test Substance Purity Medium  Metric 4: Negative and Vehicle Controls N/A Metric 5: Positive Controls N/A Metric 6: Randomized Allocation of Animals Low  Characterization Metric 7: Preparation and Storage of Test Low Substance Metric 8: Consistency of Exposure Uninformative Administration Metric 9: Reporting of Doses/Concentrations Medium Metric 10: Exposure Frequency and Duration Medium Metric 11: Number of Exposure Groups and High Dose/Concentration Spacing Metric 12: Exposure Route and Method Low  Metric 13: Test Animal Characteristics Low Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Metric 15: Number of Animals per Group Medium  Assessment

HERO ID: 5447301 Table: 5 of 5

#### ... continued from previous page

**Study Citation:** 

Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.

Health

th Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Weight change

Effect(s):
Duration:

Chemical:

Acute (less than or equal to 24 hr) Acute-Dermal 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447301

Domain	Metric	Rating	Comments
Metric 17	Consistency of Outcome Assessment	Medium	Details of outcome assessment were not reported, but animals appeared to be consistently observed
Metric 18	Sampling Adequacy	High	Not applicable since no comparisons were made; weights of surviving animals were recorded
Metric 19:	Blinding of Assessors	N/A	not necessary for study type
Metric 20:	Negative Control Response	N/A	No control is required for this assay
Domain 6: Confounding / Variable (Metric 21)	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
Metric 22	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not necessary for this study type (no controls)
Metric 24	Reporting of Data	High	Data for individual animals were reported

# **Overall Quality Determination**

Study Citation:	Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect
	initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substanc				
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	Medium	Diethylnitrosamine was used as a positive control for the tumor initiation protocol.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure Cha	racterization			
1	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	A single gavage dose appears sufficient for determination of tumor initiation potential
	36	N 1 6 F G 1	3.6.11	(similar protocol used by Pereira et al., 1982).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only a single dose level was used, but it was justified as the MTD.
	Metric 12:	Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Domain 4: Test Animals				
Domain 1. Test / minais	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome Asso	essment			
Domain J. Outcome Assi	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment was appropriate and sensitive for tumor initiation potential.
			High	Timing of necropsy was consistent across groups.
	Metric 17:	Consistency of Outcome Assessment	півіі	

HERO ID: 200479 Table: 1 of 3

#### ... continued from previous page

<b>Study Citation:</b>	Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect
	initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.
Health	Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** 

Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200479

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology review.
	Metric 20:	Negative Control Response	High	The biological response (incidence of GGT-positive foci) of the negative control group was adequate.
Domain 6: Confound	ling / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	There is no evidence of confounding variables in test design and procedures that would affect tumor initiation.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No animal attrition occurred in this experiment. There was no information either to support or dismiss the suggestion that differences among groups in other health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	High	Incidence data, with standard errors, are reported for each group in Table 3.

<b>Overall Quality</b>	Determination
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# High

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Decreased body weight gain (1,1,2-TCE only)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

112110 121	200.77			
Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Desi	ign			
	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	N/A	A positive control is not required for the endpoint of body weight.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure	e Characterization			
Domain D. Ziipoouit	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	A single gavage dose is appropriate for the kinds of short-term assays conducted for the determination of acute effects.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only a single dose level was used, but it was justified as the MTD.
	Metric 12:	Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Domain 4: Test Anii	mals			
Bonium 1. Test 7 mm	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was appropriate. Body weight, body weight gain liver weight, and liver-to-body weight ratios were measured.
	Metric 17:	Consistency of Outcome Assessment	Low	The timing of body weight and liver weight measurements was not reported.
		Contin	ued on next pa	age
			-	

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Nutritional/Metabolic

**Outcome(s):** 

Reported Health Decreased

Effect(s):

Decreased body weight gain (1,1,2-TCE only)

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol) **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200479

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	Low	Sample size for body weight, body weight gain, liver weight, and liver-to-body weight ratios was not reported.
	Metric 19:	Blinding of Assessors	N/A	The outcome (body weight) is not subjective.
	Metric 20:	Negative Control Response	Low	The biological response (body weight/liver weight) of the negative control group was not reported.
Domain 6: Confounding	g / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Food and water were provided ad libitum. There is no evidence of confounding vari- ables in test design and procedures that would affect the endpoint of body weight and liver weight.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No animal attrition was reported in this experiment. There was no information either to support or dismiss the suggestion that differences among groups in other health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	Low	Results were described only in the text. Numerical values (i.e., body weight, body weight gain, liver weight, and liver-to-body weight rations) were not provided.

### **Overall Quality Determination**

### Medium

HERO ID: 200479 Table: 3 of 3

	Study Citation:	Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect
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initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Hepatic/Liver

**Outcome(s):** 

Reported Health

Decreased absolute liver weight (1,1,2-TCE only)

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200479

HERO ID.	200479			
Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Desig	gn			
•	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	N/A	A positive control is not required for the endpoint of liver weight.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure	Characterization			
r	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	A single gavage dose is appropriate for determination of acute effects.
	Metric 11:	Number of Exposure Groups and	Medium	Only a single dose level was used, but it was justified as the MTD.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment for liver was very limited (liver weight only).
	Metric 17:	Consistency of Outcome Assessment	High	Timing of necropsy was consistent across groups.
	Metric 18:	Sampling Adequacy	Low	Sample size for liver weight measurements was not reported.
	Metric 19:	Blinding of Assessors	N/A	The outcome (liver weight) is not subjective.
	Metric 20:	Negative Control Response	Low	The biological response (liver weight) of the negative control group was not reported.

Continued on next page ...

HERO ID: 200479 Table: 3 of 3

#### ... continued from previous page

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Hepatic/Liver

**Outcome(s):** 

Reported Health

Decreased absolute liver weight (1,1,2-TCE only)

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Single dose (initiation protocol)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200479

Domain		Metric	Rating	Comments
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Food and water were provided ad libitum. There is no evidence of confounding variables in test design and procedures that would affect the endpoint of liver weight.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No animal attrition occurred in this experiment. There was no information either to support or dismiss the suggestion that differences among groups in other health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	Low	Results were described only in the text. Numerical values (i.e., absolute and relative liver weights) were not provided.

## **Overall Quality Determination**

### Medium

HERO ID: 18954 Table: 1 of 3

Study Citation: Moody, D. E., James, J. L., Clawson, G. A., Smuckler, E. A. (1981). Correlations among the changes in hepatic microsomal components after intoxication

with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693.

Health Nutritional/Metabolic

Outcome(s):

Reported Health

Body weights

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single oral dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name, a CASRN was not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was reported; a batch and/or lot number was not included. The identity was not analytically verified by the performing laboratory and could not be confirmed on the source website.
	Metric 3:	Test Substance Purity	High	The test substance was reported to be "spectro grade"
Domain 2: Test Design	ı			
	Metric 4:	Negative and Vehicle Controls	Low	A negative control was included; however, details of the control (untreated vs. vehicle) were not specified. The study tested multiple chemical compounds that were dissolved in different vehicles. It is unclear whether there was one, or many control groups.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into groups.
Domain 3: Exposure C	haracterization			
-	Metric 7:	Preparation and Storage of Test Substance	Medium	The test substance was dissolved in mineral oil. No further details regarding preparation were provided. Storage details were not specified; however, given the acute nature of the study, this is not expected to have a major impact on the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	All animals were dosed with a consistent volume of 5 ml/kg; however, there is ambiguity as to whether control animals were left untreated, or were dosed with a vehicle.
	Metric 9:	Reporting of Doses/Concentrations	High	The dose was clearly reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration (single oral dose) was appropriate for the purposes of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single dose group was used, precluding the ability to determine a dose-response, although this was not the purpose of the study. The authors reported using "relatively high doses" (0.5-2.0 times the reported LD50 values) in order to maximize the changes produced.
	Metric 12:	Exposure Route and Method	High	The exposure route and method (gavage) was appropriate and suited for the test substance.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Medium	Animal species, strain, sex, source, and starting body weights were provided. Age was not specified. The animals were appropriate for the study.
		Continu	ued on next pa	nge

Study Citation: Moody, D. E., James, J. L., Clawson, G. A., Smuckler, E. A. (1981). Correlations among the changes in hepatic microsomal components after intoxication

with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single oral dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 18954

Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Limited information on animal husbandry conditions (cage type and food) was provided. Other details were not sufficiently reported to determine whether there were differences between groups.
	Metric 15:	Number of Animals per Group	Medium	The number of animals was low (3/group), but was sufficient for statistical analysis and appeared to be appropriate for the purposes of the study.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodological details for measuring animal body weights were not provided; however, this is not expected to have a substantial impact on the study results.
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment were not reported. The timing of body weight measurements was not specified. This deficiency could have a substantial impact on the results.
	Metric 18:	Sampling Adequacy	Low	There is a lack of methodological and reporting details for this outcome of interest, it is presumed that the body weights of all animals were measured; however, this cannot be confirmed based on the data available.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcome of interest.
-	Metric 20:	Negative Control Response	Low	The negative control response for this outcome of interest was not reported.
Domain 6: Confoundi	ng / Variable Co	ntrol		
Domain o. Comodital	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly reported and appropriate for the outcomes of interest.
	Metric 24:	Reporting of Data	Medium	Negative findings were reported qualitatively in the text. Quantitative data were not provided for independent review.

### **Overall Quality Determination**

### Medium

	Study Citation:	Moody, D. E., James, J. L., Clawson, G. A., Smuckler, E. A. (1981). Correlations among the changes in hepatic microsomal components after intoxication
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with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693.

Health

Mortality

**Outcome(s): Reported Health** 

Survival

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Single oral dose Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID.	10754			
Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name, a CASRN was not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was reported; a batch and/or lot number was not included. The identity was not analytically verified by the performing laboratory and could not be confirmed on the source website.
	Metric 3:	Test Substance Purity	High	The test substance was reported to be "spectro grade"
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	Low	A negative control was included; however, details of the control (untreated vs. vehicle) were not specified. The study tested multiple chemical compounds that were dissolved in different vehicles. It is unclear whether there was one, or many control groups.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into groups.
D ' 1 E G				
Domain 3: Exposure Ch	aracterization Metric 7:	Draparation and Storage of Test	Modium	The test substance was discolved in mineral ail No further details
	Metric 7:	Preparation and Storage of Test Substance	Medium	The test substance was dissolved in mineral oil. No further details regarding preparation were provided. Storage details were not specified; however, given the acute nature of the study, this is not expected to have a major impact on the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	All animals were dosed with a consistent volume of 5 ml/kg; however, there is ambiguity as to whether control animals were left untreated, or were dosed with a vehicle.
	Metric 9:	Reporting of Doses/Concentrations	High	The dose was clearly reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration (single oral dose) was appropriate for the purpose of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single dose group was used, precluding the ability to determine a dose-response, although this was not the purpose of the study. The authors reported using "relatively high doses" (0.5-2.0 times the reported LD50 values) in order to maximize the changes produced.
	Metric 12:	Exposure Route and Method	High	The exposure route and method (gavage) was appropriate and suited for the test substance.
Domain 4: Test Animals	ı			
Zomani i. Tost / miniais	Metric 13:	Test Animal Characteristics	Medium	Animal species, strain, sex, source, and starting body weights were provided. Age was not specified. The animals were appropriate for the study.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Limited information on animal husbandry conditions (cage type and food) was provided. Other details were not sufficiently reported to determine whether there were differences between groups.

**Study Citation:** Moody, D. E., James, J. L., Clawson, G. A., Smuckler, E. A. (1981). Correlations among the changes in hepatic microsomal components after intoxication with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693.

Health

Mortality

**Outcome(s): Reported Health** 

Survival

Effect(s):

Acute (less than or equal to 24 hr) Single oral dose **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 18954

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The number of animals was low (3/group), but was sufficient for statistical analysis and appeared to be appropriate for the purposes of the study.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodological details of outcome assessment were not provided; however, for the endpoint of interest (mortality), this is not expected to have a substantial impact on results.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding the execution of the study protocol for outcome assessment were not reported; however, for the endpoint of interest (mortality), this is not expected to have a substantial impact on results.
	Metric 18:	Sampling Adequacy	High	Quantitative data were not provided for the endpoint of interest, but the reporting of results suggests that all animals were evaluated for the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Medium	The negative control response for this outcome of interest was not explicitly reported; however the text and data tables indicated that no animals died.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly reported and appropriate for the outcomes of interest.
	Metric 24:	Reporting of Data	High	Negative findings were reported qualitatively in the text.

# **Overall Quality Determination**

High

Study Citation:	Moody, D. E., James, J. L., Clawson, G. A., Smuckler, E. A. (1981). Correlations among the changes in hepatic microsomal components after intoxication with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693				
Health Outcome(s):	with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693. Hepatic/Liver				
Reported Health	Systemic: R	elative liver weightsMechanistic: measureme	ents of microsor	mal total protein. RNA content, phospholipids, and diene conjugates. Cytochrome	
Effect(s):	Systemic: Relative liver weightsMechanistic: measurements of microsomal total protein, RNA content, phospholipids, and diene conjugates. Cytochrom P-450 content, NADPH cytochrome reductase, and cytochrome B5 content were also measured along with the relative content of fatty acids from lipi				
Duration:	extracts and measurements of linoleic and arachidonic acid.  Acute (less than or equal to 24 hr) Single oral dose				
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:	18954				
Domain		Metric	Rating	Comments	
Domain 1: Test Substanc	e				
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name, a CASRN was not provided.	
	Metric 2:	Test Substance Source	Low	A commercial source was reported; a batch and/or lot number was not included. The identity was not analytically verified by the performing laboratory and could not be confirmed on the source website.	
	Metric 3:	Test Substance Purity	High	The test substance was reported to be "spectro grade"	
Domain 2: Test Design			_		
	Metric 4:	Negative and Vehicle Controls	Low	A negative control was included; however, details of the control (untreated vs. vehicle) were not specified. The study tested multiple chemical compounds that were dissolved in different vehicles. It is unclear whether there was one, or many control groups.	
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.	
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into groups.	
Domain 3: Exposure Cha		D	3.6.12		
	Metric 7:	Preparation and Storage of Test Substance	Medium	The test substance was dissolved in mineral oil. No further details regarding preparation were provided. Storage details were not specified; however, given the acute nature of the study, this is not expected to have a major impact on the study results.	
	Metric 8:	Consistency of Exposure Administration	Medium	All animals were dosed with a consistent volume of 5 ml/kg; however, there is ambiguity as to whether control animals were left untreated, or were dosed with a vehicle.	
	Metric 9:	Reporting of Doses/Concentrations	High	The dose was clearly reported.	
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration (single oral dose) was appropriate for the purposes of the study.	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single dose group was used, precluding the ability to determine a dose-response, although this was not the purpose of the study. The authors reported using "relatively high doses" (0.5-2.0 times the reported LD50 values) in order to maximize the changes produced.	
	Metric 12:	Exposure Route and Method	High	The exposure route and method (gavage) was appropriate and suited for the test substance.	
Domain 4: Test Animals					
	Metric 13:	Test Animal Characteristics	Medium	Animal species, strain, sex, source, and starting body weights were provided. Age was not specified. The animals were appropriate for the study.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Limited information on animal husbandry conditions (cage type and food) was provided Other details were not sufficiently reported to determine whether there were differences between groups.	
		Contin	ued on next pa	ge	

Study Citation:				relations among the changes in hepatic microsomal components after intoxication		
Health	with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693. Hepatic/Liver					
Outcome(s):	Hepatic/Liver					
Reported Health	Systemic: R	elative liver weightsMechanistic: measureme	ents of microsom	nal total protein RNA content, phospholipids, and diene conjugates. Cytochrom		
Effect(s):	Systemic: Relative liver weightsMechanistic: measurements of microsomal total protein, RNA content, phospholipids, and diene conjugates. Cytochroper-150 content, NADPH cytochrome reductase, and cytochrome B5 content were also measured along with the relative content of fatty acids from lextracts and measurements of linoleic and arachidonic acid. Acute (less than or equal to 24 hr) Single oral dose					
211000(8)1						
Duration:						
Chemical:	,	bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	18954					
Domain		Metric	Rating	Comments		
	Metric 15:	Number of Animals per Group	Medium	The number of animals was low (3/group), but was sufficient for statistical analysis and appeared to be appropriate for the purposes of the study.		
Domain 5: Outcome	Assessment					
	Metric 16:	Outcome Assessment Methodology	High	Methodological details for measuring relative liver weight were not provided; however, this is not expected to have a substantial impact on the study results. Outcome assessment methodologies for the mechanistic endpoints were adequately described.		
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding the execution of the study protocol for outcome assessment of liver weights were not reported. Details of the outcome assessment for mechanistic endpoin were adequately described and suggest there was consistency across groups.		
	Metric 18:	Sampling Adequacy	Medium	There is a lack of methodological and reporting details for organ weight measurements it is assumed the liver weights of all animals were weighed, although this cannot be confirmed based on the data available. Sampling for mechanistic endpoints were appropriate.		
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcome of interest.		
	Metric 20:	Negative Control Response	Medium	The negative control responses for liver weights were not provided (no quantitative data). Negative control responses for other mechanistic endpoints were adequately shown.		
Domain 6: Confound	ing / Variable Co	ntrol				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.		
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly reported and appropriate for the outcomes of interest.		
	Metric 24:	Reporting of Data	Medium	Data for an exposure-related finding (increased liver weight) was described in the text, but results were not shown. Data for mechanistic endpoints were displayed graphically and included measures of variance and indications of statistical significance.		

HERO ID: 4697223 Table: 1 of 1

1.1 Dichloroothona	

Study Citation:	Morel, G., Ban, M., Hettich, D., Huguet, N. (1999). Role of SAM-dependent thiol methylation in the renal toxicity of several solvents in mice. Journal of Applied Toxicology 19(1):47-54.					
Health	Renal/Kidney					
Outcome(s):	y					
Reported Health	Immunohistochemistry to assess damage of renal proximal tubules					
Effect(s):						
<b>Duration:</b>		han or equal to 24 hr) Acute				
Chemical:		bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	4697223					
Domain		Metric	Rating	Comments		
Domain 1: Test Substan		_ ~.				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.		
	Metric 2:	Test Substance Source	High	The source of the test substance was Merck (Darmstadt, Germany).		
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported to be >99%.		
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	The negative control group was appropriate (vehicle control).		
	Metric 5:	Positive Controls	N/A	Not applicable for this study.		
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.		
Domain 3: Exposure Ch		D	3.6.11			
	Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance preparation and storage were not adequately reported, however since this is a once time gavage study, this lack of information is unlikely to have a substantial impact on results.		
	Metric 8:	Consistency of Exposure	Low	Gavage volume was not reported.		
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.		
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were reported and appropriate for this study.		
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Selection of doses were not justified by study authors and a full range of response (both a NOAEL and LOAEL, with at least one dose above the LOAEL) were not obtained.		
	Metric 12:	Exposure Route and Method	High	Exposure route and method were appropriate.		
Domain 4: Test Animals						
	Metric 13:	Test Animal Characteristics	Medium	Age of the mice was not reported.		
	Metric 14:	Adequacy and Consistency of Animal	Medium	Not all husbandry conditions were fully reported. Study states animals were under con-		
	3.6 1.5	Husbandry Conditions	3.6.11	trolled environmental conditions but does not specify what they were.		
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group was adequate (10/group).		
Domain 5: Outcome Ass	sessment					
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest.		
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.		
	Metric 18:	Sampling Adequacy	High	Sampling was adequate.		
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary.		
		Conti	nued on nex			
Continued on next page						

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Study Citation:	Morel, G., Ban, M., Hettich, D., Huguet, N. (1999). Role of	SAM-dependent thiol methylation in th	e renal toxicity of several solvents in mice. Journal of

Applied Toxicology 19(1):47-54.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health

Immunohistochemistry to assess damage of renal proximal tubules

Effect(s):

**Duration:**Acute (less than or equal to 24 hr) Acute**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4697223

Domain		Metric	Rating	Comments
Metric 20: Negative Control Response		Medium	The negative control response was appropriate.	
Domain 6: Confound	ling / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	High	Data were fully reported.

## Overall Quality Determination High

Study Citation: Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kaut	ffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health
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Perspectives 43:41-52.

Mortality Health

**Outcome(s):** 

**Reported Health** LD50

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) acute

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID: 62637

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	test substance identified by nomenclature
	Metric 2:	Test Substance Source	High	test substance was obtained from commercial source and lot # provided
	Metric 3:	Test Substance Purity	Low	Not reported
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	N/A	Negative control not required for study type
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Used log probit analysis to determine LD50
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	preparation and storage conditions were incompletely reported but unlikely to affect results
	Metric 8:	Consistency of Exposure Administration	High	exposures were administered consistently across groups
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	doses were not reported
	Metric 10:	Exposure Frequency and Duration	High	single administration was appropriate for the study
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	number of groups and spacing were not reported but appeared sufficient to determine LD50
	Metric 12:	Exposure Route and Method	High	route route and method of exposure was suited to the test substance
Domain 4: Test Animal	2			
Domain 1. Test / minut	Metric 13:	Test Animal Characteristics	Medium	animal characteristics were reported except starting body weight, animals were obtained from a commercial source and are appropriate
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	animal husbandry conditions were reported and consistent
	Metric 15:	Number of Animals per Group	Low	not reported
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	High	assessment methodology was appropriate for the outcome of interest
	Metric 17:	Consistency of Outcome Assessment	Medium	outcome assessment appeared to be consistent across study groups
	Metric 18:	Sampling Adequacy	Low	Not reported
	Metric 19:	Blinding of Assessors	N/A	not necessary
		Conti	nued on next pag	e

HERO ID: 62637 Table: 1 of 1

#### ... continued from previous page

**Study Citation:** Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health

Perspectives 43:41-52.

Health

Mortality

**Outcome(s): Reported Health** 

LD50

Effect(s):

Acute (less than or equal to 24 hr) acute **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62637

Domain		Metric	Rating	Comments
	Metric 20: Negative Control Response		N/A	not necessary
Domain 6: Confound	ing / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	there were not reported differences among groups
	Metric 22:	and Procedures Health Outcomes Unrelated to	Medium	There was no information either to support or dismiss the suggestion that there were
	Metric 23:	Exposure Data Presentation and Analysis	High	differences among groups Used log probit analysis to determine LD50
	Metric 24:	Reporting of Data	High	data were reported for all groups by sex

## **Overall Quality Determination**

Low

Human Health Hazard Animal Toxicology Evaluation

Study Citation: I	Plaa, G.L., Larson, R.E. (1965). Relative	e nephrotoxic properties of chlorinated methane	, ethane, and ethylene derivatives in mice.	Toxicology and Applied
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Pharmacology 7(1):37-44. Renal/Kidney

Health Renal/Kidney

**Outcome(s):** 

**Reported Health** 

Urinary glucose and protein; renal histopathology

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 64411

Domain		Metric	Rating	Comments
Domain 1: Test Substance	e			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure Cha	aracterization			
Zomani di Ziiposai e dii	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	Medium	Details of exposure administration are incomplete.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and	Medium	There were minor limitation in dose spacing.
		Dose/Concentration Spacing		
	Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The source and age of the mice was not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
		Husbandry Conditions		·
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed/group was not reported as 10 in each group (Table 4 legend).
Domain 5: Outcome Ass	essment			
	Metric 16:	Outcome Assessment Methodology	Medium	Some details regarding the outcome assessment methodology were lacking (e.g how long urine was collected for).
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
		Col	ntinued on next page .	•••

### Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

Study Citation: Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health

Urinary glucose and protein; renal histopathology

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute- single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 64411

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	Medium	The sampling was adequate (all surviving mice)
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.
	Metric 20:	Negative Control Response	High	Negative control responses for urinary parameters were reported in text and were appropriate for some outcomes.
Domain 6: Confounding	/ Variable Co	ntrol		
_	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Low	Statistics analysis were not performed. Significance of increased urinary glucose or protein was determined by a cutoff number set by the authors.
	Metric 24:	Reporting of Data	Medium	Incidence data is provided for presence of urinary glucose or protein above cutoff level.  The measured level of glucose and protein would be more useful.

## **Overall Quality Determination**

### Uninformative

Study Citation:	Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied
Bruuy Chanon.	Tida, G.E., Edison, R.E. (1703). Relative hepinotoxic properties of emormated methane, entance, and emytene derivatives in finee. Toxicology and Applied

Pharmacology 7(1):37-44.

Health

Mortality

**Outcome(s):** 

Reported Health

Mortality

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 64411

HERO ID.	07711			
Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichlroroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design	ı			
	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is info mation on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure C	haracterization			
Domain 5. Exposure C	Metric 7:	Preparation and Storage of Test	Low	Preparation and storage conditions were not properly reported given the volatility of the
		Substance		test substance.
	Metric 8:	Consistency of Exposure	Medium	Details of exposure administration are incomplete.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and	Medium	There were minor limitation in dose spacing.
		Dose/Concentration Spacing		
	Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Low	The source and age of the mice was not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed/group was not reported as 10 in each group (Table 4 legend).
Domain 5: Outcome A	ssassmant			
Domain J. Outcome A	Metric 16:	Outcome Assessment Methodology	Medium	Details regarding the outcome assessment methodology were lacking.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Medium	The sampling was adequate.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.
	Wictic 19.	<del>-</del>	ntinued on next page .	

HERO ID: 64411 Table: 2 of 2

#### ... continued from previous page

Study Citation: Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44.

Health

Mortality

**Outcome(s):** 

Reported Health

Mortality

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute- single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 64411

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	Low	Negative control responses was not reported.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistics analysis were not performed but data is presented so that independent analysis can be done.
	Metric 24:	Reporting of Data	High	Mortality data is adequately presented.

# **Overall Quality Determination**

## Uninformative

HERO ID: 200568 Table: 1 of 1

1	I _I	Dic	hΙ	orget	hane

Study Citation:	Salovsky, P., Shopova, V., Dancheva, V., Yordanov, Y., Marinov, E. (2002). Early pneumotoxic effects after oral administration of 1,2-dichloroethane. Journal of Occupational and Environmental Medicine 44(5):475-480.				
Health	Lung/Respir		(3).473-460.		
Outcome(s):		···· ,			
Reported Health	Biochemical	and histological changes in lung, relative lur	ng weight; inclu	ides mechanistic endpoints	
Effect(s):		6 6		•	
<b>Duration:</b>	Acute (less t	han or equal to 24 hr) single dose			
Chemical:		bethane- Isomer: 1,2-Dichloroethane			
HERO ID:	200568				
Domain		Metric	Rating	Comments	
Domain 1: Test Substan	ce				
	Metric 1:	Test Substance Identity	High	1,2-DCE (C2H4Cl2)]; 1,2-dichloroethane; CASRN reported	
	Metric 2:	Test Substance Source	High	from Merck; batch or lot number was not identified (but material is not expected to vary in composition.)	
	Metric 3:	Test Substance Purity	Low	Purity not reported.	
Domain 2: Test Design					
	Metric 4:	Negative and Vehicle Controls	High	0.2 ml sunflower oil	
	Metric 5:	Positive Controls	N/A	Positive controls are not needed for this type of study.	
	Metric 6:	Randomized Allocation of Animals	Low	study did not report how animals were allocated to study groups	
Domain 3: Exposure Ch	aracterization				
•	Metric 7:	Preparation and Storage of Test Substance	Medium	preparation/administration of test substance is described; storage is not described. The assay is a short-term study and therefore storage is unlikely to affect results.	
	Metric 8:	Consistency of Exposure Administration	High	exposure administration were reported and exposures were administered consistently across study groups	
	Metric 9:	Reporting of Doses/Concentrations	High	0, 136 mg/kg	
	Metric 10:	Exposure Frequency and Duration	High	single dose	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	only a control and 1 dose tested; 1/5 of the median of the lethal dose; dose level was adequate to determine results for some outcomes.	
	Metric 12:	Exposure Route and Method	High	oral; gavage	
Domain 4: Test Animals	1				
Domain 1. 10st / Millians	Metric 13:	Test Animal Characteristics	High	species, strain, sex, age, and starting body weight were reported; the test animal was obtained from a commercial source	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some husbandry conditions were reported (temperature, humidity, diet, and water availability); the light- dark cycle was not reported. unlikely to have a substantial impact on results; conditions are adequate and the same for all test groups	
	Metric 15:	Number of Animals per Group	Medium	40/group	
Domain 5: Outcome Ass	sessment				
		Continu	ued on next pa	996	

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Study Citation:	Salovsky, P., Shopova, V., Dancheva, V., Yordanov, Y., Marinov, E. (2002). Early pneumotoxic effects after oral administration of 1,2-dichloroethane.
	Journal of Occupational and Environmental Medicine 44(5):475-480.

Health

Lung/Respiratory

**Outcome(s):** 

Reported Health

Biochemical and histological changes in lung, relative lung weight; includes mechanistic endpoints

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) single dose **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200568

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology addressed the intended outcomes for biochemical changes in lungs; however, outcome assessment for histological examinations were not clear. It is noted that examinations included well-described histological methods inl-cuding hematoxylin-eosin stain, can Gieson's stain and periodic acid-Schiff Hotchkiss-McManus test; no further details on assessment methodology was reported. Histological outcomes were reported in the results. Assessment methodology included timing of assessment (days 1, 5, 15, and 30) and measured endpoints were able to detect effects.
	Metric 17:	Consistency of Outcome Assessment	High	outcomes were assessed consistently across study groups
	Metric 18:	Sampling Adequacy	Medium	10 rats of each group for each day 1, 5, 15, and 30 were sacrificed. Biochemical analysis of the bronchoalveolar lavage and lung homogenate was conducted in 6 rats/group and histological examination was conducted on 4 rats/group.
	Metric 19:	Blinding of Assessors	N/A	not applicable
	Metric 20:	Negative Control Response	Low	The biological responses of the control group were adequate for BALF and lung homogenate assessment; Histological outcomes for controls were not reported.
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report information to determine confounding variables including body weight changes, food/water consumption
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There were no mortality reported and no no information regarding health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	statistical methods were described
	Metric 24:	Reporting of Data	Low	Data for exposure-related findings were presented for BALF and lung homogenate evaluation with outcomes by exposure group and day of evaluation (1, 5, 15, 30 days post-exposure); lung histology results were only presented for treated rats.

## **Overall Quality Determination**

## Medium

Study Citation:	Sherwood, R.L., O'Shea, W., Thomas, P.T., Ratajczak, H.V., Aranyi, C., Graham, J.A. (1987). Effects of inhalation of ethylene dichloride on pulmonary
	defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.

Health Immune/Hematological

Outcome(s): Reported Health

lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 3h-single dose mouse **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200590

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name.
	Metric 2:	Test Substance Source	Low	Source was not reported
	Metric 3:	Test Substance Purity	Medium	purity was not reported; "spectro grade" liquid test substance indicates high purity
Domain 2: Test Design				
· ·	Metric 4:	Negative and Vehicle Controls	High	The study authors reported using an appropriate concurrent negative control group.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	animal allocation was not reported
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test	Medium	preparation of the test substance was reported and appropriate. storage was not reported
	Metric 8:	Substance Consistency of Exposure Administration	Medium	details of exposure administration were incompletely reported but appeared to be consistent across groups
	Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and both were appropriate for this study type and the outcomes of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	number of groups and spacing was justified by previous data and was sufficient to identify a response
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were appropriate for the test substance.
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	High	test animal characteristics were all reported and obtained from commercial source
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All husbandry conditions were reported (including temperature, humidity, light-dark cycle, diet) and were adequate and the same for control and exposed groups.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (groups of 10 females) was reported, appropriate for the study type and outcome analysis, and consistent with studies of the same or similar type.
Domain 5: Outcome As	sessment			
Domain 3. Outcome As	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest and the assessment methodology was sensitive and appropriate for the outcomes of interest.

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Study Citation:	Sherwood, R.L., O'Shea, W., Thomas, P.T., Ratajczak, H.V., Aranyi, C., Graham, J.A. (1987). Effects of inhalation of ethylene dichloride on pulmonary defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.						
Health	Immune/Hei	natological					
Outcome(s):							
Reported Health	lymphocyte	stimulation, alveolar macrophage assay, pul	monary bac	tericidal activity, streptococcus aerosol challenge			
Effect(s):							
Duration:	Acute (less t	han or equal to 24 hr) 3h-single dose mouse	<b>;</b>				
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	200590						
Domain		Metric	Rating	Comments			
	Metric 17:	Consistency of Outcome Assessment	Medium	outcome assessment were previously cited and briefly described and appeared to be carried out consistently across groups			
	Metric 18:	Sampling Adequacy	High	The information supplied indicates the use of adequate sampling for the outcomes of interest.			
	Metric 19:	Blinding of Assessors	N/A	Not necessary			
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate.			
Domain 6: Confoundin	g / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	information reported was not complete, but did not indicate any differences			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss any differences			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described and sufficient data (e.g., means with standard deviations) were provided to conduct an independent statistical analysis.			
	Metric 24:	Reporting of Data	High	data were reported for all groups and outcomes, and negative data was described in text			

HERO ID: 200590 Table: 2 of 2

Study Citation:								
II M.	defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.							
Health Outcome(s):	immune/Hei	Immune/Hematological; Immune/Hematological;						
	Immuna/Har	metalogical: lymphogyto stimulation alvo	olor maara	phogo access pulmoners heateriaidal estivity etroptogogous garceal shallonger Im-				
<b>Reported Health</b> Immune/Hematological: lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challen mune/Hematological: lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge;								
Duration:		han or equal to 24 hr) 3h-single dose rat	macropnage	assay, pullionary bactericidal activity, streptococcus acrosol chancinge,				
Chemical:		pethane- Isomer: 1,2-Dichloroethane						
HERO ID:	200590	retitatie 130mer. 1,2-Diemoroethane						
Domain		Metric	Rating	Comments				
Domain 1: Test Substa	nce							
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively by name.				
	Metric 2:	Test Substance Source	Low	All Outcomes: Source was not reported				
	Metric 3:	Test Substance Purity	Medium	All Outcomes: purity was not reported; "spectro grade" liquid test substance indicates high purity				
Domain 2: Test Design	1							
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study authors reported using an appropriate concurrent negative control group.				
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type				
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: animal allocation was not reported				
Domain 3: Exposure C	'haracterization							
Domain 3. Exposure C	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: preparation of the test substance was reported and appropriate. storage was not reported				
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: details of exposure administration were incompletely reported but appeared to be consistent across groups				
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Administered doses were reported without ambiguity.				
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and both were appropriate for this study type and the outcomes of interest.				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Number of groups was adequate. Spacing was justified by previous data but was not sufficient to identify a response				
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were appropriate for the test substance.				
Domain 4: Test Anima	ıls							
Domain 7. 10st /Millia	Metric 13:	Test Animal Characteristics	High	All Outcomes: test animal characteristics were all reported and obtained from commercial source				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: All husbandry conditions were reported (including temperature, humidity, light- dark cycle, diet) and were adequate and the same for control and exposed				
	Metric 15:	Number of Animals per Group	Low	groups.  All Outcomes: The number of animals per study group (groups of 10 females) was reported, appropriate for the study type and outcome analysis, and consistent with studies of the same or similar type.				
Domain 5: Outcome A	ssessment	Conti	nued on nex	of page				

HERO ID: 200590 Table: 2 of 2

### ... continued from previous page

Study Citation:	Sherwood I	R.I. O'Shea W. Thomas P.T. Rataiczak	H V Arany	i, C., Graham, J.A. (1987). Effects of inhalation of ethylene dichloride on pulmonary				
oracj cirarion		defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.						
Health		Immune/Hematological; Immune/Hematological;						
Outcome(s):								
Reported Health	Immune/Her	matological: lymphocyte stimulation, alve	eolar macro	phage assay, pulmonary bactericidal activity, streptococcus aerosol challenge; Im				
Effect(s):	mune/Hema	tological: lymphocyte stimulation, alveolar	macrophage	assay, pulmonary bactericidal activity, streptococcus aerosol challenge;				
<b>Duration:</b>	Acute (less t	than or equal to 24 hr) 3h-single dose rat						
Chemical:	1,1-Dichloro	pethane- Isomer: 1,2-Dichloroethane						
HERO ID:	200590							
Domain		Metric	Rating	Comments				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcomes of interest and the assessment methodology was sensitive and appropriate for the outcomes of interest.				
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: outcome assessment were previously cited and briefly described and appeared to be carried out consistently across groups				
	Metric 18:	Sampling Adequacy	Low	All Outcomes: The information supplied indicates the use of adequate sampling for the outcomes of interest.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary				
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group were adequate.				
Domain 6: Confoundi	ng / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: information reported was not complete, but did not indicate any differences				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss any differences				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were described and sufficient data (e.g., means with standard deviations) were provided to conduct an independent statistical analysis.				
	Metric 24:	Reporting of Data	Medium	All Outcomes: negative data was described in text				
Overall Qual	ity Deterr	nination	High					

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Nutritional/Metabolic

Outcome(s):

Reported Health Bo

Effect(s):

Body weight; food consumption

**Duration:**Acute (less than or equal to 24 hr) Acute Inhalation**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nnce			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design	n			
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	N/A	Not necessary for acute lethality studies
	Metric 5:	Positive Controls	N/A	Not necessary for acute toxicity studies
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health
Domain 3: Exposure C				
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical.
	Metric 8:	Consistency of Exposure	Low	The study indicated that the number of rats/exposure chamber varied (from 5-12)
		Administration		
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations with animals in the chamber were checked repeatedly from "time to time" by combustion analysis. Results were reported to average better than 90% of the calculated theoretical concentrations. More than 8 exposure concentrations were tested in groups of rats over several experiments (of varying duration).
	Metric 10:	Exposure Frequency and Duration	Medium	Each exposure concentration was assessed over multiple exposure durations ranging from 0.1 hrs up to 7 hours. The exposure durations across groups varied (e.g., 0.1, 0.2, 0.3, 0.4, 0.6 hrs at 81 mg/L), but only a 7 hr exposure at 1.2 mg/L), with longer exposure times tested at lower concentrations. Most of the exposure durations varied significantly from those typically used in acute toxicity studies (e.g., 4hr inhalation exposure); this duration was used for 2/8 concentrations tested.
	Metric 11:	Number of Exposure Groups and	High	A large number of exposure groups were included (5-8 depending on the experiment).
		Dose/Concentration Spacing		The spacing seemed appropriate for the outcomes of interest.
	Metric 12:	Exposure Route and Method	Medium	Whole body 160L capacity glass walled chambers were used. The text reports constant airflows were maintained through the chamber, being ~15L/min at the lowest and 30L/min at the highest. The number of air changes/hour was not indicated.

### Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Body weight; food consumption

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute Inhalation **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 4: Test Anim	als			
	Metric 13:	Test Animal Characteristics	Medium	Albino Rats were used for single-exposure experiments. The source was clearly specified, but other details were lacking (sex, strain, body weights, age). One experiment did indicate female rats were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to the diets provided. No other data were provided.
	Metric 15:	Number of Animals per Group	Medium	For the study type, the number of animals (when provided) was appropriate if not excessive, (10-54 rats/group in one experiment, 4-6 in another experiment). The numbers/group/exposure duration was not consistent.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	The text indicates animals were observed for body weight changes, but does not provide specifics on when, or with what frequency body weight measurements were taken.
	Metric 17:	Consistency of Outcome Assessment	Medium	The text indicates that all exposed animals were observed, but descriptions of the assessment outcome do not clearly specify whether all observations/measurements were done consistently across groups.
	Metric 18:	Sampling Adequacy	High	The text indicates that all exposed animals were observed for body weight changes.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this study type
	Metric 20:	Negative Control Response	N/A	A negative control was not required for this type of assay
Domain 6: Confoundi	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure were reported. All animals were reported to be healthy at the start of the study.
	Metric 23:	Data Presentation and Analysis	N/A	Although statistical analysis would normally be appropriate for this endpoint, as an acute toxicity study, no negative control group was included.
	Metric 24:	Reporting of Data	Uninformative	Quantitative data for body weights were not reported. A decrease in body weight was noted in the text, but the exposure conditions causing this effect were not reported.

# **Overall Quality Determination**

## Uninformative

HERO ID: 62617 Table: 2 of 4

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

Death

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute Inhalation **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design				
2 1000 2 000 800	Metric 4:	Negative and Vehicle Controls	N/A	Not necessary for acute lethality studies
	Metric 5:	Positive Controls	N/A	Not necessary for acute toxicity studies
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health
Domain 3: Exposure Ch		D	Т	
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical.
	Metric 8:	Consistency of Exposure	Low	The study indicated that the number of rats/exposure chamber varied (from 5-12)
		Administration		
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations with animals in the chamber were checked repeatedly from "time to time" by combustion analysis. Results were reported to average better than 90% of the calculated theoretical concentrations. More than 8 exposure concentrations were tested in groups of rats over several experiments (of varying duration).
	Metric 10:	Exposure Frequency and Duration	Medium	Each exposure concentration was assessed over multiple exposure durations ranging from 0.1 hrs up to 7 hours. The exposure durations across groups varied (e.g., 0.1, 0.2, 0.3, 0.4, 0.6 hrs at 81 mg/L), but only a 7 hr exposure at 1.2 mg/L), with longer exposure times tested at lower concentrations. Most of the exposure durations varied significantly from those typically used in acute toxicity studies (e.g., 4hr inhalation exposure); this duration was used for 2/8 concentrations tested.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	A large number of exposure groups were included (more than 8). The purpose was to identify acute toxicity values in relation to both exposure concentration and duration. The dose groups and spacing were appropriate for this purpose.
	Metric 12:	Exposure Route and Method	Medium	Whole body 160L capacity glass walled chambers were used. The text reports constant airflows were maintained through the chamber, being ~15L/min at the lowest and 30L/min at the highest. The number of air changes/hour was not indicated.

Domain 4: Test Animals

#### ... continued from previous page

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
Health	Mortality

Outcome(s):

•

**Reported Health** 

Death

Effect(s):

**Duration:**Acute (less than or equal to 24 hr) Acute Inhalation**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	Albino Rats were used for single-exposure experiments. The source was clearly speci-
				fied, but other details were lacking (sex, strain, body weights, age).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to the diets provided. No other data were provided.
	Metric 15:	Number of Animals per Group	Medium	For the study type, the number of animals (when provided) was appropriate if not excessive, (10-54 rats/group). Numbers/group/exposure duration however was not consistent.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	The timing of outcome assessment was not clearly reported. Single exposure rats were purportedly observed for two or three weeks following exposure, but others used for examinations of "organic injury" were sacrificed at "varying times" following single exposures.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were confusing, limited, or not reported; however, this does not have a large impact on evaluating mortality and determining LD50 values.
	Metric 18:	Sampling Adequacy	High	The sampling was adequate to determine the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this study type
	Metric 20:	Negative Control Response	N/A	A negative control was not required for this type of assay
Domain 6: Confoundi	ng / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure were reported. All animals were reported to be healthy at the start of the study.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not necessary for this outcome of interest.
	Metric 24:	Reporting of Data	High	Incidences of deaths for rats was clearly reported. LC50, LC99 and LC0.01 values are plotted in relation to duration of exposure graphically.

# **Overall Quality Determination**

High

Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

HERO ID: 62617 Table: 3 of 4

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Neurological/Behavioral

**Outcome(s):** 

**Study Citation:** 

**Reported Health** 

Clinical signs

**Effect(s):** 

**Duration:**Acute (less than or equal to 24 hr) Acute Inhalation**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity ≥99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desi	ign			
	Metric 4:	Negative and Vehicle Controls	N/A	Not necessary for acute lethality studies
	Metric 5:	Positive Controls	N/A	Not necessary for acute toxicity studies
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health
Domain 3: Exposure	e Characterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical.
	Metric 8:	Consistency of Exposure Administration	Low	The study indicated that the number of rats/exposure chamber varied (from 5-12)
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations with animals in the chamber were checked repeatedly from "time to time" by combustion analysis. Results were reported to average better than 90% of the calculated theoretical concentrations. More than 8 exposure concentrations were tested in groups of rats over several experiments (of varying duration).
	Metric 10:	Exposure Frequency and Duration	Medium	Each exposure concentration was assessed over multiple exposure durations ranging from 0.1 hrs up to 7 hours. The exposure durations across groups varied (e.g., 0.1, 0.2, 0.3, 0.4, 0.6 hrs at 81 mg/L), but only a 7 hr exposure at 1.2 mg/L), with longer exposure times tested at lower concentrations. Most of the exposure durations varied significantly from those typically used in acute toxicity studies (e.g., 4hr inhalation exposure); this duration was used for 2/8 concentrations tested.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	A large number of exposure groups were included (5-8 depending on the experiment). The spacing seemed appropriate for the outcomes of interest.
	Metric 12:	Exposure Route and Method	Medium	Whole body 160L capacity glass walled chambers were used. The text reports constant airflows were maintained through the chamber, being ~15L/min at the lowest and 30L/min at the highest. The number of air changes/hour was not indicated.

Domain 4: Test Animals

#### ... continued from previous page

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Neurological/Behavioral

**Outcome(s):** 

Reported Health

Clinical signs

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute Inhalation 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Metric 15: Number of Animals per Group  Medium  No confounding variables were reported.	HERO ID:	62617			
Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Metric 15: Number of Animals per Group  Medium  In one experiment, 4-6 in another experiment). The numbers/group/exposure duration was not consistent.  Metric 16:  Medium  Medium  Medium  In one experiment, single exposure rats that survived were purportedly observed for two or three weeks following exposure. In a second experiment, exposed animals sacrificed at "varying times" following single exposures (not further specified). In third experiment, the observation period was also not reported. It is assumed that a mals were observed for clinical signs/behavior changes daily, but limited informat this endpoint is available. The protocol does not indicate how observed changes were concleded (e.g., if there was a quantitative assessment of the number of animals exhibited informat this endpoint is available. The protocol does not indicate how observed changes were concluded (e.g., if there was a quantitative assessment of the number of animals exhibited informat this endpoint is available. The protocol does not indicate how observed changes of an and there were no inconsistencies relevant to this endpoint.  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  N/A  Metric 19: Blinding of Assessors  N/A  Metric 19: Negative Control Response  Medium  Medium  No confounding variables were reported.  Metric 21: Confounding Variables in Test Design  Medium  Medium  No information on health outcomes unrelated to exposure were reported. All anim	Domain		Metric	Rating	Comments
Husbandry Conditions Number of Animals per Group  Medium  For the study type, the number of animals (when provided) was appropriate if not cessive, (10-54 rats/group in one experiment, 4-6 in another experiment). The numbers/group/exposure duration was not consistent.  Domain 5: Outcome Assessment  Metric 16:  Outcome Assessment Methodology  Medium  In one experiment, single exposure rats that survived were purportedly observed for two or three weeks following exposure. In a second experiment, exposed animals sacrificed at "varying times" following single exposures (not further specified). In third experiment, the observation period was also not reported. It is assumed that a mals were observed for clinical signs/behavior changes daily, but limited informat this endpoint is available. The protocol does not indicate how observed changes were recorded (e.g., if there was a quantitative assessment of the number of animals exhibitation of the number of animals exhibitatio	]	Metric 13:	Test Animal Characteristics	Medium	Albino Rats were used for single-exposure experiments. The source was clearly speci- fied, but other details were lacking (sex, strain, body weights, age). One experiment did indicate female rats were used.
Domain 5: Outcome Assessment  Metric 16: Outcome Assessment Methodology  Medium  In one experiment, single exposure rats that survived were purportedly observed for two or three weeks following exposure. In a second experiment, exposed animals sacrificed at "varying times" following exposure in the observation period was also not reported. It is assumed that a mals were observed for clinical signs/behavior changes daily, but limited informate this endpoint is available. The protocol does not indicate how observed changes were corded (e.g., if there was a quantitative assessment of the number of animals exhibited exposures (not not indicate how observed changes were corded (e.g., if there was a quantitative assessment of the number of animals exhibited exposures for clinical signs/behavior changes daily and there were no inconsistencies relevant to this endpoint.  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  N/A  Metric 19: Regative Control Response  Metric 20: Negative Control Response  N/A  A negative control was not required for this type of assay  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design  and Procedures  Metric 22: Medid Outcomes Unrelated to  Medium  No confounding variables were reported.  All animals were observed.  Medium  No information on health outcomes unrelated to exposure were reported. All animals were observed.	]	Metric 14:	1 3	Low	Animal husbandry information was limited to the diets provided. No other data were provided.
Metric 16: Outcome Assessment Methodology  Medium  In one experiment, single exposure rats that survived were purportedly observed for two or three weeks following exposure. In a second experiment, exposed animals sacrificed at "varying times" following single exposures (not further specified). In third experiment, the observation period was also not reported. It is assumed that a mals were observed for clinical signs/behavior changes daily, but limited informat this endpoint is available. The protocol does not indicate how observed changes were orded (e.g., if there was a quantitative assessment of the number of animals exhicitance).  Metric 17: Consistency of Outcome Assessment  Medium  Metric 18: Sampling Adequacy  High  Metric 19: Blinding of Assessors  N/A  Blinding is not necessary for this study type  Metric 20: Negative Control Response  N/A  A negative control was not required for this type of assay  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design  Medium  No confounding variables were reported.  Metric 22: Health Outcomes Unrelated to  Medium  No information on health outcomes unrelated to exposure were reported. All animals were observed on the sum of the number of animals exhicitance are recorded.  Medium  No information on health outcomes unrelated to exposure were reported. All animals were observed on the time of the number of animals exhicitance are recorded.		Metric 15:	Number of Animals per Group	Medium	For the study type, the number of animals (when provided) was appropriate if not excessive, (10-54 rats/group in one experiment, 4-6 in another experiment). The numbers/group/exposure duration was not consistent.
two or three weeks following exposure. In a second experiment, exposed animals sacrificed at "varying times" following single exposures (not further specified). In third experiment, the observation period was also not reported. It is assumed that a mals were observed for clinical signs/behavior changes daily, but limited informat this endpoint is available. The protocol does not indicate how observed changes were corded (e.g., if there was a quantitative assessment of the number of animals exhick changes)  Metric 17: Consistency of Outcome Assessment  Medium  Metric 18: Sampling Adequacy  High  All animals were observed for clinical signs/behavior changes da and there were no inconsistencies relevant to this endpoint.  Metric 19: Blinding of Assessors  N/A  Metric 20: Negative Control Response  N/A  A negative control was not required for this type of assay  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design  Medium  No confounding variables were reported.  Metric 22: Health Outcomes Unrelated to  Medium  No information on health outcomes unrelated to exposure were reported. All animals were operation on the provided in the p	Domain 5: Outcome Asses	ssment			
Metric 18: Sampling Adequacy Metric 19: Blinding of Assessors Metric 20: Negative Control Response  Metric 21: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures Metric 22: Health Outcomes Unrelated to  Medium Medium No information on health outcomes unrelated to exposure were reported. All animals were observed All animals were observed Blinding is not necessary for this study type An engative control was not required for this type of assay  Medium No confounding variables were reported.  No information on health outcomes unrelated to exposure were reported. All animals were observed Blinding is not necessary for this study type An engative control was not required for this type of assay			Outcome Assessment Methodology	Medium	In one experiment, single exposure rats that survived were purportedly observed for two or three weeks following exposure. In a second experiment, exposed animals were sacrificed at "varying times" following single exposures (not further specified). In a third experiment, the observation period was also not reported. It is assumed that animals were observed for clinical signs/behavior changes daily, but limited information on this endpoint is available. The protocol does not indicate how observed changes were recorded (e.g., if there was a quantitative assessment of the number of animals exhibiting changes)
Metric 19: Blinding of Assessors N/A Blinding is not necessary for this study type Metric 20: Negative Control Response N/A A negative control was not required for this type of assay  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  Metric 22: Health Outcomes Unrelated to Medium No information on health outcomes unrelated to exposure were reported. All anim	]	Metric 17:	Consistency of Outcome Assessment	Medium	It is assumed that all animals were observed for clinical signs/behavior changes daily, and there were no inconsistencies relevant to this endpoint.
Metric 19: Blinding of Assessors N/A Blinding is not necessary for this study type Metric 20: Negative Control Response N/A A negative control was not required for this type of assay  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  Metric 22: Health Outcomes Unrelated to Medium No information on health outcomes unrelated to exposure were reported. All anim	]	Metric 18:	Sampling Adequacy	High	All animals were observed
Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  Metric 22: Health Outcomes Unrelated to Medium No information on health outcomes unrelated to exposure were reported. All anim	]	Metric 19:		N/A	Blinding is not necessary for this study type
Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  and Procedures Metric 22: Health Outcomes Unrelated to Medium No information on health outcomes unrelated to exposure were reported. All anim		Metric 20:	Negative Control Response	N/A	A negative control was not required for this type of assay
Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  and Procedures Metric 22: Health Outcomes Unrelated to Medium No information on health outcomes unrelated to exposure were reported. All anim	Domain 6: Confounding /	Variable Cor	ntrol		
Metric 22: Health Outcomes Unrelated to Medium No information on health outcomes unrelated to exposure were reported. All anim			Confounding Variables in Test Design	Medium	No confounding variables were reported.
	j	Metric 22:	Health Outcomes Unrelated to	Medium	No information on health outcomes unrelated to exposure were reported. All animals were reported to be healthy at the start of the study.
	]	Metric 23:		N/A	Statistical analysis would have been appropriate if incidences or number of animals exhibiting specific clinical signs or behavioral changes was collected. However, this data was not reported.
Continued on next page			Con	tinued on next page	·

HERO ID: 62617 Table: 3 of 4

1,1-Dichloroethane

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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Neurological/Behavioral

Outcome(s):

**Reported Health** Clinical signs

Effect(s):

Cillical signs

**Duration:** Acute (less than or equal to 24 hr) Acute Inhalation **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Me	etric 24:	Reporting of Data	Uninformative	Quantitative data for behavioral changes were not provided precluding the ability to determine whether observations were, or were not significant. Clear results from EACH dose group/exposure condition were not reported. It is not possible to identify a lowest observed effect level from the main experiment where clinical signs/behaviors are reported. One experiment did identify the duration of exposure (in hours), at several exposure concentrations, that was with or without adverse effects, but it is not specific for any given organ/system.

## **Overall Quality Determination**

## Uninformative

HERO ID: 62617 Table: 4 of 4

Study Citation: Health Outcome(s):	laboratory ar	C., Rowe, V.K., Adams, E.M., Mccollister, D. nimals. Archives of Industrial Hygiene and Occ matological; Hepatic/Liver; Lung/Respiratory; I	upational Medicine	
Reported Health Effect(s):  Duration: Chemical: HERO ID:	histology; or (Endocrine): Acute (less t		ified cholesterol; Lui	ts. Lymph node tissues examined.; Hepatic/Liver: Gross examinations; ng/Respiratory: Gross examinations; histology; organ weights; Endocrine an weights;
Domain		Metric	Rating	Comments
Domain 1: Test Substand	ce Metric 1:	Test Substance Identity	High	All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity ≥99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design	36.4	N	27/4	
	Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: Not necessary for acute lethality studies
	Metric 5: Metric 6:	Positive Controls Randomized Allocation of Animals	N/A Low	All Outcomes: Not necessary for acute toxicity studies  All Outcomes: The study did not report how animals were allocated to groups, however all animals were reported to be in good health
Domain 2: Evnasura Ch	prostorization			
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: The study indicated that the number of rats/exposure chamber varied (from 5-12)
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: All vapor concentrations with animals in the chamber were checked repeatedly from "time to time" by combustion analysis. Results were reported to average better than 90% of the calculated theoretical concentrations. More than 8 exposure concentrations were tested in groups of rats over several experiments (of varying duration).
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Each exposure concentration was assessed over multiple exposure durations ranging from 0.1 hrs up to 7 hours. The exposure durations across groups varied (e.g., 0.1, 0.2, 0.3, 0.4, 0.6 hrs at 81 mg/L), but only a 7 hr exposure at 1.2 mg/L), with longer exposure times tested at lower concentrations. Most of the exposure durations varied significantly from those typically used in acute toxicity studies (e.g., 4hr inhalation exposure); this duration was used for 2/8 concentrations tested.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: A large number of exposure groups were included (5-8 depending on the experiment). The spacing seemed appropriate for the outcomes of interest.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Whole body 160L capacity glass walled chambers were used. The text reports constant airflows were maintained through the chamber, being ~15L/min at the lowest and 30L/min at the highest. The number of air changes/hour was not indicated.
		Cont	tinued on next page	···

HERO ID: 62617 Table: 4 of 4

	continued from previous page
Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
Health	Immune/Hematological; Hepatic/Liver; Lung/Respiratory; Endocrine (Endocrine); Renal/Kidney;
Outcome(s):	
Reported Health	Immune/Hematological: Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.; Hepatic/Liver: Gross examinations;
Effect(s):	histology; organ weights; liver lipid analysis; free and esterified cholesterol; Lung/Respiratory: Gross examinations; histology; organ weights; Endocrine
	(Endocrine): Adrenal Cortex; Renal/Kidney: Gross examinations; histology; organ weights;
<b>Duration:</b>	Acute (less than or equal to 24 hr) Acute Inhalation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

<b>HERO ID:</b> 62617	7			
Domain		Metric	Rating	Comments
Domain 4: Test Animals				
Metric	ic 13: Te	est Animal Characteristics	Medium	All Outcomes: Albino Rats were used for single-exposure experiments. The source was clearly specified, but other details were lacking (sex, strain, body weights, age). One experiment did indicate female rats were used.
Metric		dequacy and Consistency of Animal usbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to the diets provided. No other data were provided.
Metric	ic 15: N	umber of Animals per Group	Uninformative	Immune/Hematological: The number of animals in the "special group" used for examinations of this outcome was not reported.; Hepatic/Liver: The number of animals in the "special group" used for histopathology examinations was not reported.; Lung/Respiratory: The number of animals in the "special group" used for histopathology examinations was not reported.; Endocrine (Endocrine): The number of animals in the "special group" used for histopathology examinations was not reported.; Renal/Kidney: The number of animals in the "special group" used for histopathology examinations was not reported.
Domain 5: Outcome Assessmen	nt			
Metric	ic 16: O	utcome Assessment Methodology	Low	Immune/Hematological: Details of outcome assessment methods were not reported (e.g, when blood samples were collected.; Hepatic/Liver: Details of histopathology methods were not reported; Lung/Respiratory: Details of histopathology methods were not reported; Endocrine (Endocrine): Details of histopathology methods were not reported; Renal/Kidney: Details of histopathology methods were not reported
Metric	ic 17: Co	onsistency of Outcome Assessment	Low	All Outcomes: Details of the consistency the of outcome assessment were not reported.
Metric	ic 18: Sa	ampling Adequacy	Low	All Outcomes: Details regarding sampling of outcomes were not reported.
Metric	ic 19: Bl	linding of Assessors	N/A	All Outcomes: Blinding is not necessary for this study type
Metric	ic 20: N	egative Control Response	N/A	Immune/Hematological: A negative control would typically be used for serum chemistry endpoints, however, this was designed as an acute toxicity assay, and negative controls are not required for this type of assay.; Hepatic/Liver: A negative control would typically be used for histopathology endpoints, however, this was designed as an acute toxicity assay, and negative controls are not required for this type of assay; Lung/Respiratory: A negative control would typically be used for histopathology endpoints, however, this was designed as an acute toxicity assay, and negative controls are not required for this type of assay; Endocrine (Endocrine): A negative control would typically be used for histopathology endpoints, however, this was designed as an acute toxicity assay, and negative controls are not required for this type of assay; Renal/Kidney: A negative control would typically be used for histopathology endpoints, however, this was designed as an acute toxicity assay, and negative controls are not required for this type of assay

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

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Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on **Study Citation:** 

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Immune/Hematological; Hepatic/Liver; Lung/Respiratory; Endocrine (Endocrine); Renal/Kidney; Health

Outcome(s):

Effect(s):

Reported Health Immune/Hematological: Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.; Hepatic/Liver: Gross examinations;

histology; organ weights; liver lipid analysis; free and esterified cholesterol; Lung/Respiratory: Gross examinations; histology; organ weights; Endocrine

HERO ID: 62617 Table: 4 of 4

(Endocrine): Adrenal Cortex; Renal/Kidney: Gross examinations; histology; organ weights;

**Duration:** Acute (less than or equal to 24 hr) Acute Inhalation Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

meno in.	02017						
Domain		Metric	Rating	Comments			
Domain 6: Confoundi	Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: No confounding variables were reported.			
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information on health outcomes unrelated to exposure were reported. All animals were reported to be healthy at the start of the study.			
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis would normally be appropriate for this endpoint. However, as an acute toxicity assay, negative controls were not included.			
	Metric 24:	Reporting of Data	Uninformative	Immune/Hematological: Increased plasma prothrombin clotting time was reported, but the exposure conditions (e.g., dose and duration) causing these effects were not reported.; Hepatic/Liver: Histopathological changes were noted, but the exposure conditions (e.g., dose and duration) causing these effects were not reported.; Lung/Respiratory: Histopathological changes were noted, above a specific concentration, however, since each exposure concentration was tested at multiple durations, it is not known at which duration(s) effects were observed.; Endocrine (Endocrine): Histopathological changes were noted, but the exposure conditions (e.g., dose and duration) causing these effects were not reported.; Renal/Kidney: Histopathological changes were noted, but the exposure conditions (e.g., dose and duration) causing these effects were not reported.			

### **Overall Quality Determination**

### Uninformative

luman	Health	Hazard	Anımal	Ioxico	logy	Evaluation	

Study	Citation:

Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.

Health

Mortality

Outcome(s):

**Reported Health** LD50

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute oral **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6569955

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
Me	tric 1:	Test Substance Identity	High	Test material: 1,2-dichloroethane (ethylene dichloride). The CASRN was provided.
Me	etric 2:	Test Substance Source	High	The test material was obtained from "the specialty chemical division" of the Stauffer Chemical Company.
Me	etric 3:	Test Substance Purity	Low	The purity was not reported.
Domain 2: Test Design				
C	tric 4:	Negative and Vehicle Controls	N/A	Negative controls are not necessary for the study type.
Me	tric 5:	Positive Controls	N/A	Not necessary for the study type.
Me	tric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characte	erization			
	etric 7:	Preparation and Storage of Test Substance	Medium	Limited information on preparation (20% solution in water) was provided. Details on storage were not reported, although this is unlikely to have a major impact on an acute duration study.
Me	tric 8:	Consistency of Exposure	Low	Gavage volumes were not reported.
Me	etric 9:	Administration Reporting of Doses/Concentrations	High	Doses were clearly reported. The reported doses are likely target doses. Analytical determinations are not always made for acute gavage studies.
Me	etric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type.
Me	etric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups was appropriate for the purposes of the study.
Me	etric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.
Domain 4: Test Animals				
Me	etric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and initial body weights were provided. The age and source of the animals was not specified.
Me	etric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
Me	tric 15:	Number of Animals per Group	Medium	The study used 5 animals/group.

#### Domain 5: Outcome Assessment

#### ... continued from previous page

**Study Citation:** Health

Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.

Mortality

**Outcome(s):** 

**Reported Health** 

Effect(s):

LD50

**Duration:** Acute (less than or equal to 24 hr) Acute oral Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6569955

Domain	Metric	Rating	Comments
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
Metric 17:	Consistency of Outcome Assessment	High	The outcomes were assessed consistently across study groups.
Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest.
Metric 19:	Blinding of Assessors	N/A	Not necessary for the study type.
Metric 20:	Negative Control Response	N/A	No negative control group.
Domain 6: Confounding / Variable C		Low	The study did not report information to determine confounding.
Wietric 21:	and Procedures	Low	The study and not report information to determine confounding.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	High	The method used for LD50 calculation was not specified. However, the number of deaths per treatment group were reported and an independent statistical analysis could be conducted.
Metric 24:	Reporting of Data	Medium	Incidence of mortality in each group was reported. The time and/or causes of deaths were not specified.

# **Overall Quality Determination**

## Medium

Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.					
Health	Missing 'other' target organ					
Outcome(s):						
Reported Health	Gross patho	logy - no specific methods reported				
Effect(s):						
Duration:	,	than or equal to 24 hr) Acute oral				
Chemical: HERO ID:	6569955	bethane- Isomer: 1,2-Dichloroethane				
neko id:	0309933					
Domain		Metric	Rating	Comments		
Domain 1: Test Substa		T. (C.I.)	TT: 1			
	Metric 1:	Test Substance Identity	High	Test material: 1,2-dichloroethane (ethylene dichloride). The CASRN was provided.		
	Metric 2:	Test Substance Source	High	The test material was obtained from "the specialty chemical division" of the Stauffer Chemical Company.		
	Metric 3:	Test Substance Purity	Low	The purity was not reported.		
Domain 2: Test Design	1					
· ·	Metric 4:	Negative and Vehicle Controls	N/A	As the gross necropsy was performed as part of the LD50 study, negative controls are not necessary for the study type.		
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.		
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.		
Domain 3: Exposure C	Characterization					
	Metric 7:	Preparation and Storage of Test Substance	Medium	Limited information on preparation (20% solution in water) was provided. Details on storage were not reported, although this is unlikely to have a major impact on an acute duration study.		
	Metric 8:	Consistency of Exposure	Low	Gavage volumes were not reported.		
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were clearly reported. The reported doses are likely target doses. Analytical determinations are not always made for acute gavage studies.		
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type		
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups was appropriate for the purposes of the study.		
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.		
Domain 4: Test Anima	ıls					
Zoman ii 100t i millio	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and initial body weights were provided. The age and source of the animals was not specified.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.		
	Metric 15:	Number of Animals per Group	Medium	The study used 5 animals/group.		
Domain 5: Outcome A	ssessment					
	Metric 16:	Outcome Assessment Methodology	Low	The methodology used for gross pathological observation was not clearly reported.		
	Metric 17:	Consistency of Outcome Assessment	High	The outcomes were assessed consistently across study groups.		

HERO ID: 6569955 Table: 2 of 3

#### ... continued from previous page

Study Citation: Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.

Health Missing 'other' target organ

Outcome(s):

Reported Health

Gross pathology - no specific methods reported

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute oral **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6569955

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the study type.
	Metric 20:	Negative Control Response	N/A	No negative control group.
Domain 6: Confoundi	ng / Variable Con Metric 21: Metric 22:	Confounding Variables in Test Design and Procedures Health Outcomes Unrelated to	Low Medium	The study did not report information to determine confounding.  There was no information either to support or dismiss the suggestion that there were
		Exposure		differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Study focused on pathology findings.
	Metric 24:	Reporting of Data	Medium	There was limited reporting on the results. Results were reported in text as appearing normal but specific details or were not provided.

# **Overall Quality Determination**

## Medium

HERO ID: 6569955 Table: 3 of 3

**Study Citation:** 

Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.

Health

Neurological/Behavioral

**Outcome(s):** 

**Reported Health** 

Signs of depression and ataxia

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute oral **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6569955

HERO ID.	0507755			
Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			
	Metric 1:	Test Substance Identity	High	Test material: 1,2-dichloroethane (ethylene dichloride). The CASRN was provided.
	Metric 2:	Test Substance Source	High	The test material was obtained from "the specialty chemical division" of the Stauffer Chemical Company.
	Metric 3:	Test Substance Purity	Low	The purity was not reported.
Domain 2: Test Desi	an			
Domain 2. Test Desi	Metric 4:	Negative and Vehicle Controls	N/A	As the observation of changes in neurological/behavioral effects were part of the LD50
				study, negative controls are not necessary for the study type.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Characterization			
•	Metric 7:	Preparation and Storage of Test Substance	Medium	Limited information on preparation (20% solution in water) was provided. Details on storage were not reported, although this is unlikely to have a major impact on an acute duration study.
	Metric 8:	Consistency of Exposure	Low	Gavage volumes were not reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were clearly reported. The reported doses are likely target doses. Analytical determinations are not always made for acute gavage studies.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups was appropriate for the purposes of the study.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.
Domain 4: Test Anii	nale			
Domain 4. Test Ami	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and initial body weights were provided. The age and source of the animals was not specified.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Medium	The study used 5 animals/group.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	The methodology used to determine depression and ataxia was not reported.
	Metric 17:	Consistency of Outcome Assessment	Low	As no methodology was reported, it is impossible to determine consistency if the method was applied consistently.
		Contin	ued on next pa	10°
		Contin	uea on next pa	ıge

# Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

**Study Citation:** 

Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.

Health

Neurological/Behavioral

**Outcome(s):** 

**Reported Health** 

Signs of depression and ataxia

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute oral **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6569955

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the study type.
	Metric 20:	Negative Control Response	N/A	No negative control group.
Domain 6: Confound	ling / Variable Co Metric 21: Metric 22:	ntrol Confounding Variables in Test Design and Procedures Health Outcomes Unrelated to Exposure	Low Medium	The study did not report information to determine confounding.  There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Study focused on observations of ataxia and depression
	Metric 24:	Reporting of Data	Low	Results were reported in text but with limited details. The mean scores of ataxia/depression were not reported for each study group.

# **Overall Quality Determination**

## Medium

Study Citation:		., Conolly, R. B. (1983). Comparative in vi	ivo genotoxi	city and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-			
Health	1494. In vivo geno	toxicity (In vivo genotoxicity)					
Outcome(s):							
Reported Health	In vivo geno	In vivo genotoxicity (DNA damage) in hepatic tissue					
Effect(s):	III vivo geno	in vivo genotoxicity (DNA damage) in nepatic tissue					
Duration:	Acute (less t	han or equal to 24 hr) In vivo genotoxicity					
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	5549990	ethane- isomer. 1,2-Diemoroethane					
	3349990	Matria	D -4:	Community			
Domain  Domain 1: Test Substance		Metric	Rating	Comments			
Domain 1: Test Substant		T4 C-1 -4 I4-4	III: _L				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.			
	Metric 2:	Test Substance Source	High	The source of the test substance was MCB, Cincinnati, OH. The batch/lot number were not reported, but the purity was verified by the lab.			
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported as >99.0.			
Domain 2: Test Design							
8	Metric 4:	Negative and Vehicle Controls	High	Negative controls were treated with corn oil (vehicle)			
	Metric 5:	Positive Controls	Medium	Positive control was included.			
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.			
Domain 3: Exposure Ch	aracterization						
1	Metric 7:	Preparation and Storage of Test	Medium	Preparation and storage were not adequately described given the volatility of the test			
		Substance		substance, however, the substance was only administered as a single acute dose, and			
				therefore, storage is unlikely to affect results.			
	Metric 8:	Consistency of Exposure	Medium	Details of exposure were limited; however, this is unlikely to substantially impact re-			
		Administration		sults.			
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only nominal doses were reported.			
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate for this study type.			
	Metric 11:	Number of Exposure Groups and	High	Then number of exposure groups and doses were adequate to elicit full range of re-			
		Dose/Concentration Spacing		sponses.			
	Metric 12:	Exposure Route and Method	High	Route of exposure was appropriate (i.p injection)			
Domain 4: Test Animals							
	Metric 13:	Test Animal Characteristics	Low	The source of the test animals was not reported.			
	Metric 14:	Adequacy and Consistency of Animal	Medium	Husbandry conditions were not sufficiently reported, but unlikely to have substantial			
	metric 11.	Husbandry Conditions	Mediani	impacts.			
	Metric 15:	Number of Animals per Group	Medium	Only 6 animals per group were used.			
Domain 5: Outcome Ass	sessment						
Domain J. Outcome Ass	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate			
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across groups.			
	Metric 17.	Sampling Adequacy	High				
	wienie 10.	Samping Adequacy	High	Sampling was adequate for outcomes of interest.			

#### ... continued from previous page

<b>Study Citation:</b>	Storer, R. D., Conolly, R. B. (1983).	Comparative in vivo genotoxicity and acute hepatotoxicity	of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-
	1404		

**Outcome(s):** 

1494. In vivo genotoxicity (In vivo genotoxicity) Health

Reported Health

In vivo genotoxicity (DNA damage) in hepatic tissue

**Effect(s): Duration:** 

Acute (less than or equal to 24 hr) In vivo genotoxicity

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 5549990

Domain	Metric	Rating	Comments
Metri	: 19: Blinding of Assessors	N/A	Blinding was not necessary for this study.
Metri	20: Negative Control Response	High	Negative control response was appropriate.
Domain 6: Confounding / Varia Metri		Medium	Study did not report all information to determine confounding, reported information did not identify differences.
Metri		Medium	Study did not report all information to determine confounding, reported information did not identify differences.
Metri	1	High	Statistical analysis was appropriate.
Metri	24. Reporting of Data	High	Exposure related outcomes were reported

## **Overall Quality Determination**

## High

Storer, R. D., Conolly, R. B. (1983). Comparative in vivo genotoxicity and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-

HERO ID: 5549990 Table: 2 of 4

**Study Citation:** 

Health Hepatic/Liver Outcome(s): Reported Health Relative liver weight, serum levels of L-iditol dehydrogenase (SDH) and alanine aminotransferase (AAT or ALT) Effect(s): **Duration:** Acute (less than or equal to 24 hr) Acute toxicity Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane HERO ID: 5549990 Metric Domain Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Test substance was identified as 1,2-dichloroethane. Metric 2: Test Substance Source High The source of the test substance was MCB, Cincinnati, OH. The batch/lot number were not reported, but the purity was verified by the lab. Metric 3: Test Substance Purity High The purity of the test substance was reported as >99.0. Domain 2: Test Design Metric 4: Negative and Vehicle Controls Low It Is not clear if negative controls were untreated or received the vehicle. Metric 5: Positive Controls N/A Positive control was not needed. Metric 6: Randomized Allocation of Animals Low The study did not report how animals were allocated. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium Preparation and storage were not adequately described given the volatility of the test Substance substance, however, the substance was only administered as a single acute dose, and therefore, storage is unlikely to affect results. Metric 8: Consistency of Exposure Medium Details of exposure were limited; however, this is unlikely to substantially impact results. Administration Metric 9: Reporting of Doses/Concentrations Medium Only nominal doses were reported. Metric 10: **Exposure Frequency and Duration** High Exposure frequency and duration were reported and appropriate for this study type. Metric 11: Number of Exposure Groups and High Then number of exposure groups and doses were adequate to elicit full range of re-Dose/Concentration Spacing sponses. Exposure Route and Method Metric 12: High Route of exposure was appropriate (i.p injection) Domain 4: Test Animals Metric 13: Test Animal Characteristics Low The source of the test animals was not reported. Metric 14: Adequacy and Consistency of Animal Medium Husbandry conditions were not sufficiently reported, but unlikely to have substantial **Husbandry Conditions** impacts. Metric 15: Number of Animals per Group Medium Only 5 animals per group were used. Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology Medium Organ weight and serum chemistry was evaluated, but no histology was performed. Metric 17: Consistency of Outcome Assessment High Outcomes were assessed consistently across groups. Metric 18: Sampling Adequacy High Sampling was adequate for outcomes of interest. Blinding of Assessors Metric 19: N/A Blinding was not necessary for this study. Metric 20: Negative Control Response High Negative control response was appropriate. Continued on next page ...

HERO ID: 5549990 Table: 2 of 4

#### ... continued from previous page

Study Citation: Storer, R. D., Conolly, R. B. (1983). Comparative in vivo genotoxicity and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-

494.

**Health** Hepatic/Liver

**Outcome(s):** 

Reported Health

Relative liver weight, serum levels of L-iditol dehydrogenase (SDH) and alanine aminotransferase (AAT or ALT)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute toxicity **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5549990

Domain		Metric	Rating	Comments
Domain 6: Confounding	g / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Study did not report all information to determine confounding, reported information did not identify differences.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	Medium	Most exposure related outcomes were reported (absolute wt not reported).

## **Overall Quality Determination**

## Medium

HERO ID: 5549990 Table: 3 of 4

Study Citation: Storer, R. D., Conolly, R. B. (1983). Comparative in vivo genotoxicity and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-

1494. Mortality

Health
Outcome(s):

**Reported Health** 

Mortality

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute toxicity **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5549990

Domain		Metric	Rating	Comments
Domain 1: Test Substa				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	The source of the test substance was MCB, Cincinnati, OH. The batch/lot number were not reported, but the purity was verified by the lab.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported as >99.0.
Domain 2: Test Design	n			
C	Metric 4:	Negative and Vehicle Controls	Low	It Is not clear if negative controls were untreated or received the vehicle.
	Metric 5:	Positive Controls	N/A	Positive control was not needed.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure C	Characterization			
•	Metric 7:	Preparation and Storage of Test Substance	Medium	Preparation and storage were not adequately described given the volatility of the test substance, however, the substance was only administered as a single acute dose, and therefore, storage is unlikely to affect results.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure were limited; however, this is unlikely to substantially impact results.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only nominal doses were reported.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate for this study type.
	Metric 11:	Number of Exposure Groups and	Medium	Minor limitations (full range of responses was not obtained)
		Dose/Concentration Spacing		
	Metric 12:	Exposure Route and Method	High	Route of exposure was appropriate (i.p injection)
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Low	The source of the test animals was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not sufficiently reported, but unlikely to have substantial impacts.
	Metric 15:	Number of Animals per Group	Medium	Only 5 animals per group were used.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Assessment methodology was appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate for outcomes of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	Negative control response was appropriate.

HERO ID: 5549990 Table: 3 of 4

1,1-Dichloroethane

#### ... continued from previous page

Study Citation: Storer, R. D., Conolly, R. B. (1983). Comparative in vivo genotoxicity and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-

1494. Mortality

**Outcome(s):** 

**Reported Health** 

Mortality

Effect(s): Duration:

Chemical:

Health

Acute (less than or equal to 24 hr) Acute toxicity 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5549990

Domain		Metric	Rating	Comments		
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Study did not report all information to determine confounding, reported information did not identify differences.		
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed but all data is presented to conduct independent statistics.		
	Metric 24:	Reporting of Data	High	Exposure related outcomes were reported.		

## **Overall Quality Determination**

## High

Storer, R. D., Conolly, R. B. (1983). Comparative in vivo genotoxicity and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-

HERO ID: 5549990 Table: 4 of 4

**Study Citation:** 

Health	1494. Renal/Kidne	NV.					
Outcome(s):	Renai/Kiune	ey .					
Reported Health	Relative kidney weight and blood urea level (BUN)						
Effect(s):	Relative kiulicy weight and blood urea level (BOIV)						
Duration:	Acute (less than or equal to 24 hr) Acute toxicity						
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	5549990						
Domain		Metric	Rating	Comments			
Domain 1: Test Subst							
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.			
	Metric 2:	Test Substance Source	High	The source of the test substance was MCB, Cincinnati, OH. The batch/lot number were not reported, but the purity was verified by the lab.			
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported as >99.0.			
Domain 2: Test Desig	'n						
Domain 2. Test Desig	Metric 4:	Negative and Vehicle Controls	Low	It Is not clear if negative controls were untreated or received the vehicle.			
	Metric 5:	Positive Controls	N/A	Positive control was not needed.			
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.			
Domain 3: Exposure (	Characterization						
Domain 3. Exposure	Metric 7:	Preparation and Storage of Test	Medium	Preparation and storage were not adequately described given the volatility of the test			
	Wedle 7.	Substance Substance	Wedium	substance, however, the substance was only administered as a single acute dose, and therefore, storage is unlikely to affect results.			
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure were limited; however, this is unlikely to substantially impact results.			
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only nominal doses were reported.			
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate for this study type.			
	Metric 11:	Number of Exposure Groups and	Medium	Minor limitations (full range of responses was not obtained) for renal (BUN).			
		Dose/Concentration Spacing					
	Metric 12:	Exposure Route and Method	High	Route of exposure was appropriate (i.p injection)			
Domain 4: Test Anim	als						
	Metric 13:	Test Animal Characteristics	Low	The source of the test animals was not reported.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not sufficiently reported, but unlikely to have substantial impacts.			
	Metric 15:	Number of Animals per Group	Medium	Only 5 animals per group were used.			
Domain 5: Outcome A	A academant						
Domain 5: Outcome A	Assessment Metric 16:	Outcome Assessment Methodology	Medium	Once weight and common chamistry was avaluated but no histology was norfamed			
	Metric 17:	Outcome Assessment Methodology Consistency of Outcome Assessment	High	Organ weight and serum chemistry was evaluated, but no histology was performed.  Outcomes were assessed consistently across groups.			
	Metric 18:	Sampling Adequacy		Sampling was adequate for outcomes of interest.			
	Metric 19:	Blinding of Assessors	High N/A	Blinding was not necessary for this study.			
	Metric 20:	Negative Control Response	High	Negative control response was appropriate.			
	MEHIC 20.						
		Continu	ued on next pa	age			

Human Health Hazard Animal Toxicology Evaluation HERO ID: 5549990 Table: 4 of 4

## ... continued from previous page

**Study Citation:** Storer, R. D., Conolly, R. B. (1983). Comparative in vivo genotoxicity and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-

Health Renal/Kidney

**Outcome(s):** 

**Reported Health** 

Relative kidney weight and blood urea level (BUN)

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute toxicity Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5549990

Domain		Metric	Rating	Comments		
Domain 6: Confounding / Variable Control						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Study did not report all information to determine confounding, reported information did not identify differences.		
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.		
	Metric 24:	Reporting of Data	Medium	Most exposure related outcomes were reported (absolute wt not reported).		

# **Overall Quality Determination**

# Medium

HERO ID: 200613 Table: 1 of 2

Domain 4: Test Animals

Metric 13:

Test Animal Characteristics

Study Citation:	Storer, R.D., Conolly, R.B. (1985). An investigation of the role of microsomal oxidative metabolism in the in vivo genotoxicity of 1,2-dichloroetha Toxicology and Applied Pharmacology 77(1):36-46.							
Health	Renal/Kidne	ey; Hepatic/Liver;						
Outcome(s): Reported Health	Renal/Kidne	: Kidney weight; Hepatic/Liver: Liver weight, serum IDH (L-iditol (also called sorbitol) dehydrogenase), and alanine aminotransferase;						
Effect(s):								
<b>Duration:</b>	Acute (less	than or equal to 24 hr) Acute IP						
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane							
HERO ID:	200613							
Domain		Metric	Rating	Comments				
Domain 1: Test Substance	ce							
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified by name (1,2-Dichloroethane); CASRN was not provided.				
	Metric 2:	Test Substance Source	High	All Outcomes: A commercial source was identify, and the test substance was verified by GC by the performing laboratory.				
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity confirmed by GC and reported to be 99.9%				
D : 0 T . D :								
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control groups consisted of sham treated animals administered corn oil (vehicle), and animals administered a piperonyl butoxide pre-treatment, followed by a corn-oil (vehicle) treatment.				
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not required for acute-duration studies.				
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animal allocation was not reported.				
Domain 3: Exposure Ch			3.6.11					
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Test substance storage was not reported, but as this is an acute study, it is unlikely to significantly impact the results. Preparation of the test solution was adequately described.				
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Details of exposure administration of the test substance were reported (constant volume of 5 mL/kg); volumes injected of corn oil controls was not explicitly stated.				
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Single-dose acute study; the single dose was appropriate for the purposes of the study				
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Single ip dose was appropriate for the purposes of the study				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: It seems like data from previous studies and from their lab were used to determine the appropriate dose.				
	Metric 12:	Exposure Route and Method	High	Renal/Kidney: The exposure route was generally appropriate for evaluating the acute				

## Continued on next page ...

Medium

endpoints reported.; Hepatic/Liver: The exposure route was generally appropriate for

All Outcomes: Animal species, strain, sex, age, and source were reported. Starting body

evaluating the acute endpoints reported

weights were not provided.

		···contin	ued from p	revious page		
Study Citation: Health	Storer, R.D., Conolly, R.B. (1985). An investigation of the role of microsomal oxidative metabolism in the in vivo genotoxicity of 1,2-dichloroethane. Toxicology and Applied Pharmacology 77(1):36-46. Renal/Kidney; Hepatic/Liver;					
Outcome(s):		•				
Reported Health Effect(s):	Renal/Kidney: Kidney weight; Hepatic/Liver: Liver weight, serum IDH (L-iditol (also called sorbitol) dehydrogenase), and alanine aminotransferase;					
<b>Duration:</b>	Acute (less than or equal to 24 hr) Acute IP					
Chemical:		ethane- Isomer: 1,2-Dichloroethane				
HERO ID:	200613					
Domain		Metric	Rating	Comments		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Animal husbandry conditions reported included: temperature, light-dark cycle, diet, water availability; humidity was not provided. Conditions were adequate and the same for control and exposed populations, such that the only difference was exposure.		
	Metric 15:	Number of Animals per Group	Medium	Renal/Kidney: The study included 3-5 animals/group, numbers were sufficient for statistical analysis.; Hepatic/Liver: The study included 3-5 animals/group (acute toxicity) or 4-12/group (in vivo genotoxicity) numbers were sufficient for statistical analysis.		
Domain 5: Outcome As	ssessment					
	Metric 16:	Outcome Assessment Methodology	High	Renal/Kidney: All animals were sacrificed 24hrs post-treatment and methods details were adequately provided.; Hepatic/Liver: All animals were sacrificed 4-24hrs post-treatment depending on the endpoint and methods details were adequately provided.		
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: All groups were evaluated consistently for the outcomes of interest		
	Metric 18:	Sampling Adequacy	High	All Outcomes: All animals were evaluated; sampling was adequate for statistical analysis and the outcome of interest.		
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this study type		
	Metric 20:	Negative Control Response	High	All Outcomes: Control responses appeared to be appropriate		
Domain 6: Confoundin	a / Variable Co	atral				
Domain o. Comountum	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.		
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were clearly described and appropriate.		
	Metric 24:	Reporting of Data	High	Renal/Kidney: Results were clearly reported (Means +/- SD); Hepatic/Liver: Results were clearly reported (Means +/- SD); glutathione time course data were presented in a figure.		
Overall Quali	ty Detern	nination	High			

Study Citation: Storer, R.D., Conolly, R.B. (1985). An investigation of the role of microsomal oxidative metabolism in the in vivo genotoxicity of 1,2-dichloroethane.

Toxicology and Applied Pharmacology 77(1):36-46.

Health

in vivo genotoxcity (in vivo genotoxicity)

**Outcome(s):** 

**Reported Health** 

Double-stranded DNA breaks in hepatic DNA from mice treated in vivo.

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute IP **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by name (1,2-Dichloroethane); CASRN was not provided.
	Metric 2:	Test Substance Source	High	A commercial source was identify, and the test substance was verified by GC by the performing laboratory.
	Metric 3:	Test Substance Purity	High	Purity confirmed by GC and reported to be 99.9%
Domain 2: Test Design				
Domain 2. Test Besign	Metric 4:	Negative and Vehicle Controls	High	Control groups consisted of sham treated animals administered corn oil (vehicle), and animals administered a piperonyl butoxide pre-treatment, followed by a corn-oil (vehicle) treatment.
	Metric 5:	Positive Controls	N/A	Although positive controls are generally required for genotoxicity studies, based on previous studies, this test substance is a known genotoxic agent and this study was focused on understanding the mechanism of genotoxicity rather than evaluating genotoxicity potential. Therefore, a positive control was not needed for the purposes of this study.
	Metric 6:	Randomized Allocation of Animals	Low	Animal allocation was not reported.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance storage was not reported, but as this is an acute study, it is unlikely to sig nificantly impact the results. Preparation of the test solution was adequately described.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration of the test substance were reported (constant volume of 5 mL/kg); volumes injected of corn oil controls was not explicitly stated.
	Metric 9:	Reporting of Doses/Concentrations	High	Single-dose acute study; the single dose was appropriate for the purposes of the study
	Metric 10:	Exposure Frequency and Duration	High	Single ip dose was appropriate for the purposes of the study
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	it seems like data from previous studies and from their lab were used to determine the appropriate dose.
	Metric 12:	Exposure Route and Method	High	The exposure route was generally appropriate for evaluating the acute endpoints reported
Domain 4: Test Animals				
Domain 4. Test Allillidis	Metric 13:	Test Animal Characteristics	Medium	Animal species, strain, sex, age, and source were reported. Starting body weights were not provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Animal husbandry conditions reported included: temperature, light- dark cycle, diet, water availability; humidity was not provided. Conditions were adequate and the same for control and exposed populations, such that the only difference was exposure.

		contin	ued from p	revious page			
Study Citation: Health	Storer, R.D., Conolly, R.B. (1985). An investigation of the role of microsomal oxidative metabolism in the in vivo genotoxicity of 1,2-dichloroethane. Toxicology and Applied Pharmacology 77(1):36-46. in vivo genotoxicity (in vivo genotoxicity)						
Outcome(s): Reported Health Effect(s):	Double-strar	Double-stranded DNA breaks in hepatic DNA from mice treated in vivo.					
Duration:	Acute (less t	han or equal to 24 hr) Acute IP					
Chemical:		pethane- Isomer: 1,2-Dichloroethane					
HERO ID:	200613						
Domain		Metric	Rating	Comments			
	Metric 15:	Number of Animals per Group	Medium	The study included 3-5 animals/group (acute toxicity) or 4-12/group (in vivo genotoxicity) numbers were sufficient for statistical analysis.			
Domain 5: Outcome A	Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	The methods details were adequately provided. The methods used were narrow in scope and only detected single strand breaks in alkali. The study authors indicated that if the test substance (or its metabolite) did not lead to formation of alkali-labile lesions, then other types of damage would not be detected by the DNA damage assay used.			
	Metric 17:	Consistency of Outcome Assessment	High	All groups were evaluated consistently for the outcomes of interest			
	Metric 18:	Sampling Adequacy	High	All animals were evaluated; sampling was adequate for statistical analysis and the outcome of interest.			
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type			
	Metric 20:	Negative Control Response	High	Control responses appeared to be appropriate			
Domain 6: Confoundi	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate.			
	Metric 24:	Reporting of Data	High	Results were clearly reported (Means +/- SD) with the number of mice in each group reported.			
Overall Qual	ity Detern	nination	High				

HERO ID: 200614 Table: 1 of 8

Study Citation: Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral, intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health
Outcome(s):

in vivo genotoxicity (Genotoxicity); in vivo genotoxicity (Genotoxicity);

Reported Health

in vivo genotoxicity (Genotoxicity): Hepatic DNA damage; in vivo genotoxicity (Genotoxicity): Hepatic DNA damage;

Effect(s):

**Duration:**Acute (less than or equal to 24 hr) acute-oral**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200614

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Substance identity reported by nomenclature.
	Metric 2:	Test Substance Source	High	in vivo genotoxicity (Genotoxicity): Test substance obtained from commercial source and analytically confirmed "obtained from MCB Manufacturing Chemists Inc. Cincinnati OH".; in vivo genotoxicity (Genotoxicity): Test substance obtained from commercial source and analytically confirmed "obtained from MCB Manufacturing Chemists Inc. Cincinnati OH.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance purity confirmed to be >99.9% by GCMS.
Domain 2: Test Design				
S	Metric 4:	Negative and Vehicle Controls	High	in vivo genotoxicity (Genotoxicity): Vehicle control, corn oil, was appropriate. CCl4 administered by i.p. injection served as a negative control substance.; in vivo genotoxicity (Genotoxicity): Vehicle control, corn oil, was appropriate.
	Metric 5:	Positive Controls	Medium	All Outcomes: DMN administered by a single i.p. injection served as a positive control.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animal allocation was not reported.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	in vivo genotoxicity (Genotoxicity): Storage was not reported, though this is unlikely to impact results given the short-term nature of the study. Details of preparation in corn oil were limited.; in vivo genotoxicity (Genotoxicity): Storage was not reported, though this is unlikely to impact results given the short-term nature of the study. Details of preparation in corn oil and saline were limited.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure administration was consistent across groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	in vivo genotoxicity (Genotoxicity): A single administration was appropriate.; in vivo genotoxicity (Genotoxicity): Single administration was appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	in vivo genotoxicity (Genotoxicity): The number of exposure groups was adequate and spacing covered the range of effect.; in vivo genotoxicity (Genotoxicity): Number of exposure groups was adequate and spacing covered the range of effect.
	Metric 12:	Exposure Route and Method	High	in vivo genotoxicity (Genotoxicity): The oral route was suited to the test substance.; in vivo genotoxicity (Genotoxicity): Route was suited to the test substance.

Domain 4: Test Animals

		contin	ued from p	revious page			
Study Citation:	intraperitone	Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral, intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.					
Health	in vivo geno	toxicity (Genotoxicity); in vivo genotoxicity	y (Genotoxio	city);			
Outcome(s):							
Reported Health	in vivo genotoxicity (Genotoxicity): Hepatic DNA damage; in vivo genotoxicity (Genotoxicity): Hepatic DNA damage;						
Effect(s):							
Duration:		Acute (less than or equal to 24 hr) acute-oral					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	200614						
Domain		Metric	Rating	Comments			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Test animal characteristics were mostly reported, except starting body weight. Animals were reported to be obtained from a commercial source or bred in house.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported and appropriate.			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: Number of animals (4-8) was sufficient for the study type and outcome.			
Domain 5: Outcome	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methodology addressed the outcome of interest, DNA damage.			
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Assessment was consistent across study groups.			
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for the outcome of interest.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary.			
	Metric 20:	Negative Control Response	High	All Outcomes: Negative controls responded appropriately.			
Domain 6: Confound	•						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding, but reported information did not indicate differences.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	in vivo genotoxicity (Genotoxicity): There was no information either to support or dismiss differences among groups.; in vivo genotoxicity (Genotoxicity): There was no information either to support or dismiss differences across groups.			
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistics were reported and appropriate.			
	Metric 24:	Reporting of Data	High	in vivo genotoxicity (Genotoxicity): Data were reported for all groups: table 3.; in vivo genotoxicity (Genotoxicity): Data were reported for all groups: tables 3 and 4.			
Overall Qua	lity Detern	nination	High				

HERO ID: 200614 Table: 2 of 8

**Study Citation:** Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral,

intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

in vivo genotoxicity (Genotoxicity)

**Outcome(s):** 

**Reported Health** 

Hepatic DNA damage

Effect(s):

Acute (less than or equal to 24 hr) Inhalation, acute **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substance	e			
	Metric 1:	Test Substance Identity	High	Substance identity reported by nomenclature.
	Metric 2:	Test Substance Source	High	Test substance obtained from commercial source and analytically confirmed "obtained from MCB Manufacturing Chemists Inc. Cincinnati OH".
	Metric 3:	Test Substance Purity	High	Test substance purity confirmed to be >99.9% by GCMS.
Domain 2: Test Design				
_	Metric 4:	Negative and Vehicle Controls	High	Room air control was appropriate.
	Metric 5:	Positive Controls	Medium	DMN administered by a single i.p. injection served as a positive control.
	Metric 6:	Randomized Allocation of Animals	Low	Animal allocation was not reported.
Domain 3: Exposure Cha	racterization			
-	Metric 7:	Preparation and Storage of Test	Medium	Details of inhalation chamber preparation were limited.
	Metric 8:	Substance Consistency of Exposure	High	Exposure administration was consistent across groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	Medium	Single 4h administration was appropriate.
	Metric 11:	Number of Exposure Groups and	High	Number of exposure groups was adequate and spacing covered the range of effect.
		Dose/Concentration Spacing	Ü	
	Metric 12:	Exposure Route and Method	High	Route was suited to the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Test animal characteristics were mostly reported, except starting body weight. Animals were reported to be obtained from a commercial source or bred in house.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported and appropriate.
	Metric 15:	Number of Animals per Group	Medium	Number of animals (4-8) was sufficient for the study type and outcome.
Domain 5: Outcome Asse	essment			
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology addressed the outcome of interest, DNA damage.
	Metric 17:	Consistency of Outcome Assessment	High	Assessment was consistent across study groups.
	Metric 18:	Sampling Adequacy	High	sampling was adequate for the outcome of interest.
		1 0	-	
	Metric 19:	Blinding of Assessors	N/A	Not necessary.

HERO ID: 200614 Table: 2 of 8

1,1-Dichloroethane

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**Study Citation:** Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral,

intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

in vivo genotoxicity (Genotoxicity)

**Outcome(s):** 

**Reported Health** 

Hepatic DNA damage

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Inhalation, acute **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200614

Domain		Metric	Rating	Comments			
Domain 6: Confounding / Variable Control							
	Metric 21:	Confounding Variables in Test Design	Medium	The study did not report all information to determine confounding, but reported informa-			
		and Procedures		tion did not indicate differences.			
	Metric 22:	Health Outcomes Unrelated to	Medium	High mortality was observed at high doses where DNA damage was observed, but lower			
		Exposure		dose groups were also included in the study.			
	Metric 23:	Data Presentation and Analysis	High	Statistics were reported and appropriate.			
	Metric 24:	Reporting of Data	High	Data were reported for all groups: table 3.			

# **Overall Quality Determination**

# High

HERO ID: 200614 Table: 3 of 8

**Study Citation:** Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral, intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Hepatic/Liver; Renal/Kidney;

**Outcome(s):** 

**Reported Health** 

Hepatic/Liver: liver weight, clinical chem, hepatic DNA damage; Renal/Kidney: kidney weight, clinical chem;

Effect(s):

Acute (less than or equal to 24 hr) acute-oral **Duration:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 200614

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Hepatic/Liver: Substance identify reported by nomenclature.; Renal/Kidney: Substance identity was reported by nomenclature.
	Metric 2:	Test Substance Source	High	All Outcomes: Test substance was obtained from a commercial source and analytically confirmed.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance purity was confirmed to be >99%.
Domain 2: Test Design	gn			
·	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Vehicle control was appropriate.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animal allocation was not reported.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Hepatic/Liver: Storage was not reported, though this is unlikely to impact results given the short-term nature of the study. Details of preparation in in corn oil and saline were limited.; Renal/Kidney: Storage not reported, though this is unlikely to impact results given the short-term nature of the study. Details of preparation in corn oil were limited.
	Metric 8:	Consistency of Exposure Administration	High	Hepatic/Liver: Exposure administration was consistent across groups.; Renal/Kidney: Exposure administration was consistent across groups
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Hepatic/Liver: A single oral administration is appropriate for evaluation of acute effects.; Renal/Kidney: A single oral administration was appropriate for evaluation of acute effects.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups was adequate and spacing covered the range of effect.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route was suited to the test substance.
Domain 4: Test Anim	าลไร			
Zomani i. Tost Milli	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Test animal characteristics were mostly reported except starting body weight. Animals were reported to be obtained from a commercial source or bred in house.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported and appropriate.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals was sufficient for the study type and outcome.

Domain 5: Outcome Assessment

HERO ID: 200614 Table: 3 of 8

## ... continued from previous page

Study Citation:	Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral,
TT 1/1	intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Hepatic/Liver; Renal/Kidney; **Outcome(s):** 

**Reported Health** 

Hepatic/Liver: liver weight, clinical chem, hepatic DNA damage; Renal/Kidney: kidney weight, clinical chem;

**Effect(s):** 

Acute (less than or equal to 24 hr) acute-oral **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200614

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Outcome assessment methodology partially addressed the outcome.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Assessment was consistent across study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary.
	Metric 20:	Negative Control Response	High	All Outcomes: Negative controls responded appropriately.
Domain 6: Confounding	/ Variable Con Metric 21:	trol Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding, but reported information did not indicate differences.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss differences among groups.
	Metric 23:	Data Presentation and Analysis	High	Hepatic/Liver: Statistics were reported and appropriate; Renal/Kidney: Statistics were reported and appropriate.
	Metric 24:	Reporting of Data	High	Hepatic/Liver: Data were reported for all groups; Renal/Kidney: Data were reported for all groups.

# **Overall Quality Determination**

# High

HERO ID: 200614 Table: 4 of 8

**Study Citation:** Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral,

intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

death

Effect(s):

Acute (less than or equal to 24 hr) acute-oral **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200614

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Substance identity reported by nomenclature.
	Metric 2:	Test Substance Source	High	Test substance obtained from commercial source and analytically confirmed.
	Metric 3:	Test Substance Purity	High	Test substance purity was confirmed to be >99%.
Domain 2: Test Design				
Č	Metric 4:	Negative and Vehicle Controls	High	Vehicle control was appropriate.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	Animal allocation was not reported.
Domain 3: Exposure C	haracterization			
Bollium 3. Exposure C.	Metric 7:	Preparation and Storage of Test Substance	Low	Storage not reported, though this is unlikely to impact results given the short-term nature of the study. Details of preparation in corn oil were limited.
	Metric 8:	Consistency of Exposure	High	Exposure administration was consistent across groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Single exposure was appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups was adequate. Spacing was insufficient to identify an effect on mortality, but the goal of the study was to identify sublethal acute effects.
	Metric 12:	Exposure Route and Method	High	The route was suited to the test substance.
Domain 4: Test Animal	le.			
Domain 4. Test Amma	Metric 13:	Test Animal Characteristics	Medium	Test animal characteristics were mostly reported except starting body weight. Animals were reported to be obtained from a commercial source or bred in house.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Most husbandry conditions were reported and appropriate.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Medium	Number of animals was sufficient for the study type and outcome.
Domain 5: Outcome A	ssessment			
2 omain 5. Outcome 7 i	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology addressed the outcome.
	Metric 17:	Consistency of Outcome Assessment	High	Assessment was consistent across study groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate.
	Metric 19:	Blinding of Assessors	N/A	Not necessary.
	Metric 20:	Negative Control Response	High	Negative controls responded appropriately.

Study Citation: Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral,

intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

death

Effect(s): Duration:

Chemical:

Acute (less than or equal to 24 hr) acute-oral 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200614

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable C	ontrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding, but reported information did not indicate differences.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss differences among groups.
Metric 23:	Data Presentation and Analysis	High	Data were reported sufficiently for statistical analysis.
Metric 24:	Reporting of Data	High	Data were reported for all groups.

High

# **Overall Quality Determination**

HERO ID: 200614 Table: 5 of 8

**Study Citation:** Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral,

intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

death

Effect(s):

Acute (less than or equal to 24 hr) acute-i.p. **Duration:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 200614

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ance			
	Metric 1:	Test Substance Identity	High	Substance identity reported by nomenclature.
	Metric 2:	Test Substance Source	High	Test substance obtained from commercial source and analytically confirmed.
	Metric 3:	Test Substance Purity	High	Test substance purity confirmed to be >99%.
Domain 2: Test Desig	n			
	Metric 4:	Negative and Vehicle Controls	High	Vehicle control was appropriate.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	Animal allocation was not reported.
Domain 3: Exposure (	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	Storage was not reported, though this is unlikely to impact results given the short-term nature of the study. Details of preparation in corn oil were limited.
	Metric 8:	Consistency of Exposure	High	Exposure administration was consistent across groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Single exposure was appropriate.
	Metric 11:	Number of Exposure Groups and	High	Number of exposure groups and spacing was adequate
		Dose/Concentration Spacing	C	
	Metric 12:	Exposure Route and Method	High	Route was suited to the test substance.
Domain 4: Test Anim	als			
Bonian 1. Test 7 mm	Metric 13:	Test Animal Characteristics	Medium	Test animal characteristics were mostly reported except starting body weight. Animals were reported to be obtained from a commercial source or bred in house.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Most husbandry conditions were reported and appropriate.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Medium	Number of animals was sufficient for the study type and outcome.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology addressed the outcome.
	Metric 17:	Consistency of Outcome Assessment	High	Assessment was consistent across study groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate for the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	Not necessary.
	Metric 20:	Negative Control Response	High	Negative controls responded appropriately.

HERO ID: 200614 Table: 5 of 8

## ... continued from previous page

Study Citation: Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral,

intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Mortality

**Outcome(s):** 

Reported Health

death

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) acute-i.p. **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200614

Domain		Metric	Rating	Comments
Domain 6: Confounding / Va	ariable Con	trol		
Me	etric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding, but reported information did not indicate differences.
Me	etric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss differences across groups.
Me	etric 23:	Data Presentation and Analysis	High	Data were reported sufficiently for statistical analysis.
Me	etric 24:	Reporting of Data	High	Data were reported for all groups.

# **Overall Quality Determination**

# High

Study Citation:	Storer, R.D., Jackson, N.M., Conolly, R.B. (1984).	In vivo genotoxicity and acute hepatotoxicity of 1,2-dichl	oroethane in mice: Comparison of oral,
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intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Renal/Kidney; Hepatic/Liver;

Outcome(s): Reported Health

Renal/Kidney: kidney weight, clinical chem; Hepatic/Liver: liver weight, clinical chem, hepatic DNA damage;

Effect(s):

**Duration:**Acute (less than or equal to 24 hr) acute-i.p.**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Metric 2: Test Substance Source High All Outcome firmed.	Comments  Demos: Substance identity reported by nomenclature.  Demos: Test substance obtained from commercial source and analytically condems: Test substance purity confirmed to be >99%.
Metric 1: Test Substance Identity High All Outcome Metric 2: Test Substance Source High All Outcome firmed.	omes: Test substance obtained from commercial source and analytically con-
Metric 2: Test Substance Source High All Outcome firmed.	omes: Test substance obtained from commercial source and analytically con-
firmed.	·
	omes: Test substance purity confirmed to be >99%.
Metric 3: Test Substance Purity High All Outc	
Domain 2: Test Design	
-	omes: Vehicle control was appropriate.
	dney: Not necessary for the study type.; Hepatic/Liver: ccl4 was used as a control for liver
Metric 6: Randomized Allocation of Animals Low All Outc	omes: Animal allocation was not reported.
Domain 3: Exposure Characterization	
Metric 7: Preparation and Storage of Test Medium All Outc	omes: Storage was not reported, though this is unlikely to impact results given term nature of the study. Details of preparation in corn oil were limited.
, ,	omes: Exposure administration was consistent across groups.
Administration Metric 9: Reporting of Doses/Concentrations High All Outc	omes: Doses were reported without ambiguity.
	dney: Single administration is appropriate.; Hepatic/Liver: A single administra- propriate for evaluation of acute effects.
Dose/Concentration Spacing of effect	dney: Number of exposure groups was adequate and spacing covered the range; Hepatic/Liver: The number of exposure groups was adequate and spacing he range of effect.
Metric 12: Exposure Route and Method High Renal/K	dney: Route was suited to the test substance.; Hepatic/Liver: The route was the test substance.
Domain 4: Test Animals	
Metric 13: Test Animal Characteristics Medium All Outc	omes: Test animal characteristics were mostly reported except starting body Animals were reported to be obtained from a commercial source or bred in
Metric 14: Adequacy and Consistency of Animal Medium All Outc Husbandry Conditions	omes: Most husbandry conditions were reported and appropriate.
	omes: Number of animals was sufficient for the study type and outcome.
Domain 5: Outcome Assessment	
	omes: Outcome assessment methodology partially addressed the outcome.
Continued on next page	

Study Citation:	Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral,								
Health		intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.  Renal/Kidney; Hepatic/Liver;							
	Kenai/Kidne	y, nepauc/Liver,							
Outcome(s):	D 1/17:1	Panel/Vidnov kidnov vojekt alipiael sham Hanetie/Liver kiver vojekt alipiael sham hanetie DNA demogra							
Reported Health	Renal/Kidney: kidney weight, clinical chem; Hepatic/Liver: liver weight, clinical chem, hepatic DNA damage;								
Effect(s):									
Duration:	Acute (less than or equal to 24 hr) acute-i.p.								
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane								
HERO ID:	200614								
Domain		Metric	Rating	Comments					
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Assessment was consistent across study groups.					
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for the outcome of interest.					
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary.					
	Metric 20:	Negative Control Response	High	All Outcomes: Negative controls responded appropriately.					
Domain 6. Confound	ina / Variabla Car	ntuo!							
Domain 6: Confound			3.6 11						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding, but reported information did not indicate differences.					
	Metric 22:	Health Outcomes Unrelated to	Medium	•					
	Metric 22.		Mediuiii	All Outcomes: There was no information either to support or dismiss differences across groups.					
	Metric 23:	Exposure	High						
		Data Presentation and Analysis	High	All Outcomes: Statistics were reported and appropriate.					
	Metric 24:	Reporting of Data	High	All Outcomes: Data were reported for all groups.					

Study Citation:	Storer, R.D., Jackson, N.M., Conolly, R.B. (1984).	In vivo genotoxicity and acute hepatotoxicity of 1.2-dichloroethane in mice: Comparison of oral.

Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute he intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Mortality; Renal/Kidney;

Outcome(s): Reported Health

Mortality: death; Renal/Kidney: kidney weight, clinical chem;

Effect(s):

**Duration:**Acute (less than or equal to 24 hr) Inhalation, acute**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	200614			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Substance identity reported by nomenclature.
	Metric 2:	Test Substance Source	High	All Outcomes: Test substance obtained from commercial source and analytically confirmed.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance purity confirmed to be >99%.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	Mortality: The negative control was appropriate.; Renal/Kidney: Air only control was appropriate.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animal allocation was not reported.
Domain 3: Exposure Ch	aracterization			
Domain 5. Exposure Cir	Metric 7:	Preparation and Storage of Test	Medium	All Outcomes: Details of inhalation chamber preparation were limited.
	Metric 8:	Substance Consistency of Exposure	High	All Outcomes: Exposure administration was consistent across groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Mortality: A single 4h exposure was appropriate; Renal/Kidney: A single 4h exposure was appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The number of exposure groups was adequate and spacing did not encompass effect as mortality went from none to most within 1 dose.
	Metric 12:	Exposure Route and Method	High	All Outcomes: Route was suited to the test substance.
D ' 4 T ( A ' 1				
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Test animal characteristics were mostly reported except starting body weight. Animals were reported to be obtained from a commercial source or bred in house.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported and appropriate.
	Metric 15:	Number of Animals per Group	Medium	Mortality: Number of animals was sufficient for the study type and outcome.; Renal/Kidney: The number of animals was sufficient for the study type and outcome.
Damain 5: C :				
Domain 5: Outcome As	Metric 16:	Outcome Assessment Methodology	Medium	Mortality: Outcome assessment methodology addressed the outcome.; Renal/Kidney: Outcome assessment methodology partially addressed the outcome.

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Study Citation:	Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of ora intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.							
Health	Mortality; Renal/Kidney;							
Outcome(s):								
Reported Health	Mortality: death; Renal/Kidney: kidney weight, clinical chem;							
Effect(s):								
Duration:	Acute (less than or equal to 24 hr) Inhalation, acute							
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane							
HERO ID:	200614							
Domain		Metric	Rating	Comments				
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Assessment was consistent across study groups.				
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for the outcome of interest.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary.				
	Metric 20:	Negative Control Response	High	All Outcomes: Negative controls responded appropriately.				
Domain 6: Confoundi	ng / Variable Coi	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding, but reported information did not indicate differences.				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Mortality: There was no information either to support or dismiss differences across groups.; Renal/Kidney: There was no information either to support or dismiss differences among groups.				
	Metric 23:	Data Presentation and Analysis	High	Mortality: Data were sufficient for statistical analysis.; Renal/Kidney: Statistics were reported and appropriate.				
	Metric 24:	Reporting of Data	High	All Outcomes: Data were reported for all groups.				

Study Citation: Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1.2-dichloroethane in mice: Compari
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intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

Health

Hepatic/Liver

**Outcome(s):** 

**Reported Health** 

liver weight, clinical chem, hepatic DNA damage

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Inhalation, acute **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200614

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Substance identity reported by nomenclature.
	Metric 2:	Test Substance Source	High	Test substance obtained from commercial source and analytically confirmed.
	Metric 3:	Test Substance Purity	High	Test substance purity confirmed to be >99%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Air only control was appropriate.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	Animal allocation was not reported.
D	L			
Domain 3: Exposure Cl		D	M - J:	
	Metric 7:	Preparation and Storage of Test	Medium	Details of inhalation chamber preparation were limited.
	Metric 8:	Substance Consistency of Exposure	Medium	Exposure administration was consistent across groups, control was room air.
		Administration		
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	4h single exposure was appropriate.
	Metric 11:	Number of Exposure Groups and	Medium	The number of exposure groups was adequate and spacing did not encompass effect as mortality went from none to most within 1 dose.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	The route was suited to the test substance.
		1	<u> </u>	
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	Medium	Test animal characteristics were mostly reported except starting body weight. Animcals were reported to be obtained from a commercial source or bred in house.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Most husbandry conditions were reported and appropriate.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Medium	The number of animals was sufficient for the study type and outcome.
Domain 5: Outcome As	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Outcome assessment methodology partially addressed the outcome.
	Metric 17:	Consistency of Outcome Assessment	High	Assessment was consistent across study groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate for the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	Not necessary.
	Metric 20:	Negative Control Response	High	Negative controls responded appropriately

HERO ID: 200614 Table: 8 of 8

## ... continued from previous page

Study Citation: Storer, R.D., Jackson, N.M., Conolly, R.B. (1984). In vivo genotoxicity and acute hepatotoxicity of 1,2-dichloroethane in mice: Comparison of oral, intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.

**Health** Hepatic/Liver

**Outcome(s):** 

Reported Health

liver weight, clinical chem, hepatic DNA damage

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Inhalation, acute **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200614

Domain		Metric	Rating	Comments
Domain 6: Confounding / Va	ariable Con	trol		
M	Ietric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding, but reported information did not indicate differences.
M	Ietric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss differences among groups.
M	Ietric 23:	Data Presentation and Analysis	High	Statistics were reported and appropriate.
M	letric 24:	Reporting of Data	High	Data were reported for all groups.

# Overall Quality Determination High

<b>Study Citation:</b>	Umezu, T., Shibata, Y. (2014). Different behavioral effect dose-response profiles in mice exposed to two-carbon chlorinated hydrocarbons: influence of
	structural and physical properties. Toxicology and Applied Pharmacology 279(2):103-112

Health Neurological/Behavioral

**Outcome(s):** 

**Reported Health** Righting reflex test, Bridge test, FR20 operant test and MULT operant test

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) Acute- 1,2-Dichloroethane

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was Wako Pure Chemical Industries (Osaka, Japan). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Low	Negative controls were included and appropriate (vehicle) for all behavioral tests except the righting reflex test. A negative control was not included for this test.
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure C	haracterization			
1	Metric 7:	Preparation and Storage of Test Substance	Low	Storage and preparation conditions were not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure Administration	High	Test substance was administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses are reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate (single i.p injection).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose spacing were appropriate.
	Metric 12:	Exposure Route and Method	High	Exposure route was appropriate (i.p injection).
Domain 4: Test Animal	le			
Domain 4. Test / minus	Metric 13:	Test Animal Characteristics	High	Animal characteristics were adequately reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Humidity was not reported; all other husbandry conditions were reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed per group were reported.
Domain 5: Outcome As	ssessment			
2 cmain 5. Outcome 11	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology were appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment protocols were reported and consistently assessed across the study groups.
				Or

HERO ID: 5554867 Table: 1 of 2

## ... continued from previous page

Study Citation: Umezu, T., Shibata, Y. (2014). Different behavioral effect dose-response profiles in mice exposed to two-carbon chlorinated hydrocarbons: influence of structural and physical properties. Toxicology and Applied Pharmacology 279(2):103-112.

Health

Neurological/Behavioral

Outcome(s):

**Reported Health** 

Righting reflex test, Bridge test, FR20 operant test and MULT operant test

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute- 1,2-Dichloroethane

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5554867

Domain	Metric	Rating	Comments
Metr	c 19: Blinding of Assessors	N/A	Blinding was not necessary for this study.
Metr	c 20: Negative Control Response	High	Negative control group responses were appropriate.
Domain 6: Confounding / Varia	ble Control c 21: Confounding Variables in '	Test Design Medium	Study did not report all information to determine confounding, reported information did
	and Procedures	C	not identify differences.
Metr	c 22: Health Outcomes Unrelated Exposure	I to Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metr	c 23: Data Presentation and Anal	ysis High	Statistical analysis was appropriate.
Metr	c 24: Reporting of Data	High	Data for exposure related finds were reported.

# **Overall Quality Determination**

# High

HERO ID: 5554867 Table: 2 of 2

Study Citation: Umezu, T., Shibata, Y. (2014). Different behavioral effect dose-response profiles in mice exposed to two-carbon chlorinated hydrocarbons: influence of structural and physical properties. Toxicology and Applied Pharmacology 279(2):103-112.

Health

Mortality

Outcome(s): Reported Health

24 hour lethality

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) Acute- 1,2-Dichloroethane

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ince			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was Wako Pure Chemical Industries (Osaka, Japan).
				Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	N/A	Acute lethality, negative control was not necessary.
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
	11100110 01	1 miles   1 mile	20	The study did not report now animals were unocuted.
Domain 3: Exposure C	Characterization			
	Metric 7:	Preparation and Storage of Test	Low	Storage and preparation conditions were not adequately described given the volatility of
		Substance		the test substance.
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	Ціah	Doses are reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate (single i.p injection).
			High	
	Metric 11:	Number of Exposure Groups and	High	The number of exposure groups and dose spacing were appropriate.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	Uiah	Evenosyma mouto vyga ammuomiota (i.m. inication)
	Metric 12:	Exposure Route and Method	High	Exposure route was appropriate (i.p injection).
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	High	Animal characteristics were adequately reported.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Humidity was not reported; all other husbandry conditions were reported.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed per group were reported.
Domain 5: Outcome A				
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology were appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment protocols were reported and consistently assessed across the study groups.
	Metric 18:	Sampling Adequacy	High	The number of animals evaluated were reported and adequate.
			_	Blinding was not necessary for this study.
	Metric 19:	Blinding of Assessors	N/A	Binding was not necessary for this study.

HERO ID: 5554867 Table: 2 of 2

1,1-Dichloroethane

## ... continued from previous page

**Study Citation:** Umezu, T., Shibata, Y. (2014). Different behavioral effect dose-response profiles in mice exposed to two-carbon chlorinated hydrocarbons: influence of

structural and physical properties. Toxicology and Applied Pharmacology 279(2):103-112.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

24 hour lethality

Effect(s):

Acute (less than or equal to 24 hr) Acute- 1,2-Dichloroethane **Duration:** 

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5554867

Domain		Metric	Rating	Comments
Domain 6: Confounding	g / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
-	Metric 24:	Reporting of Data	High	Data for exposure related finds were reported.

# **Overall Quality Determination**

# High

Wang, G., Yuan, Y., Zhang, J., Gao, L., Tan, X., Yang, G., Lv, X., Jin, Y. (2014). Roles of aquaporins and matrix metalloproteinases in mouse brain edema

HERO ID: 4453007 Table: 1 of 1

**Study Citation:** 

Study Citation:	formation in	duced by subacute exposure to 1,2-dichloroeth		and Teratology 44:105-112.			
Health	Mortality; N	eurological/Behavioral;					
Outcome(s):							
Reported Health	Mortality: In part one, after 3 days of exposure, the mortality rates of mice in group A to C were 0%, 30% and 60%, respectively, and the live mice ingroup						
Effect(s):				-dependent manner. In part two, the mortalityrates of mice in group D to			
				oned above became more severealong with the prolonged exposure time.			
				wo.; Neurological/Behavioral: Part 1: Body tremors and forelimb flexure;			
D			RNA and protein expr	ession of aquaporin 4, MMP2 and MMP9 in cerebral tissue;			
Duration: Chemical:		han or equal to 24 hr) Part 2: 1.2 g/m3 1 day bethane- Isomer: 1,2-Dichloroethane					
Chemical: HERO ID:	4453007	bethane- Isomer. 1,2-Dichioroethane					
	4433007	M-4-:-	D -4:	Comments			
Domain  Domain 1: Test Substan		Metric	Rating	Comments			
Jomain 1: Test Substan	ce Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.			
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance and/or batch/lot number were not pro-			
	Wieure 2.	Test Substance Source	Low	vided.			
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was more than 99% pure.			
Domain 2: Test Design							
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: Details regarding the negative control are limited and unclear if mice			
	Wietife 1.	regulive and venicle controls	Low	sham treated.			
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.			
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly divided into groups.			
Domain 3: Exposure Ch	aracterization						
1	Metric 7:	Preparation and Storage of Test	Low	All Outcomes: Given the volatility of the test substance, the study did not adequately			
		Substance		report how test substance was prepared or stored.			
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure was administered consistently across study groups.			
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	All Outcomes: Only target concentrations were reported.			
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Exposure duration was only 3.5 hours/day.			
	Metric 11:	Number of Exposure Groups and	Medium	All Outcomes: Only one concentration was studied; concentration was justified based of			
		Dose/Concentration Spacing		effects in previous findings.			
	Metric 12:	Exposure Route and Method	Uninformative	All Outcomes: A static inhalation chamber was used.			
Domain 4: Test Animals	S						
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age was not reported.			
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were adequately reported.			
		Husbandry Conditions	-				
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed /group were appropriate for the study type (n=6).			
Domain 5: Outcome Ass	sessment						

Continued on next page ...
Page 386 of 955

not adequately reported.; Neurological/Behavioral: Data were adequately reported.

## Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

Study Citation:	Wang, G., Yuan, Y., Zhang, J., Gao, L., Tan, X., Yang, G., Lv, X., Jin, Y. (2014). Roles of aquaporins and matrix metalloproteinases in mouse brain edema
Stady Classical	formation induced by subacute exposure to 1,2-dichloroethane. Neurotoxicology and Teratology 44:105-112.
Health	Mortality; Neurological/Behavioral;
Outcome(s):	
Reported Health	Mortality. In part one after 3 days of exposure, the mortality rates of mice in group A to C were 0%, 30% and 60%, respectively, and the live mice ingroup

**Effect(s):**Mortality: In part one, after 3 days of exposure, the mortality rates of mice in group A to C were 0%, 30% and 60%, respectively, and the live mice ingroup B and C showed body tremors and forelimb flexure in a time dependent and dose-dependent manner. In part two, the mortality rates of mice in group D to F were 5%, 10% and 25%, respectively. The poisoned symptoms in mice mentioned above became more severealong with the prolonged exposure time.

There was not any abnormality in the control mice after exposure in part one and two.; Neurological/Behavioral: Part 1: Body tremors and forelimb flexure; brain weight, brain water content, histology of brainPart 2: RNA and protein expression of aquaporin 4, MMP2 and MMP9 in cerebral tissue;

**Duration:** Acute (less than or equal to 24 hr) Part 2: 1.2 g/m3 1 day

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4453007

Domain	Metric	Rating	Comments
Metric 1	6: Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodology were appropriate
Metric 1	7: Consistency of Outcome Assessment	Medium	All Outcomes: Details of outcome assessment protocol were limited
Metric 1	8: Sampling Adequacy	High	All Outcomes: The number of animals evaluated/group was appropriate.
Metric 1	9: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
Metric 2	O: Negative Control Response	High	All Outcomes: The negative control response was appropriate.
Domain 6: Confounding / Variable	Control		
Metric 2	Confounding Variables in Test Design     and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.
Metric 2	2: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric 2		High	All Outcomes: Statistical analysis was performed and appropriate.
Metric 2	4: Reporting of Data	Medium	Mortality: Mortality data are reported for all groups but data on poisoned symptoms are

# **Overall Quality Determination**

## Uninformative

You-xin, Z.Q. (2010). Toxic encephalopathy induced by occupational exposure to 1,2-dichloroethane and toxicological effect on animal model. :89-93.

HERO ID: 4492125 Table: 1 of 2

**Study Citation:** 

Health	Mortality; N	Nortality;	1	
Outcome(s): Reported Health	Mortality, m	nortality; Mortality: mortality;		
Effect(s):	Mortanty: II	iortanty, Mortanty: mortanty;		
Duration:	Acute (less t	than or equal to 24 hr) varying concentrations		
Chemical:		pethane- Isomer: 1,2-Dichloroethane		
HERO ID:	4492125			
Domain		Metric	Rating	Comments
Domain 1: Test Substa				
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was not reported. Batch or lot number was not reported.
	Metric 3:	Test Substance Purity	Low	All Outcomes: Purity of test substance was not reported.
Domain 2: Test Desig	n			
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A negative control group was sham-treated.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Study reports that animals were randomly allocated into groups.
Domain 3: Exposure (	Characterization			
	Metric 7:	Preparation and Storage of Test	Low	All Outcomes: Preparation and storage were not adequately described given the volatil-
		Substance		ity of the test substance.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Test substance was delivered consistently across study groups.
	Matria O.	Administration	Low	All Outs and Astrology and the state of the
	Metric 9: Metric 10:	Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were reported and appropriate for this study type.
	Metric 11:	Number of Exposure Groups and	Medium	All Outcomes: Number of exposure groups/spacing were adequate.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	Medium	All Outcomes: The number of air changes/hour were not reported.
		r		
Domain 4: Test Anima				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age of animals was not reported.
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were adequately reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Medium	All Outcomes: The number of animals/group was acceptable.
	Within 13.	rumoer of rumnars per Group	Wicaram	An Outcomes. The number of animas/group was acceptable.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Mortality: The outcome assessment methodology was appropriate.; Mortality: The outcome assessment methodology appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for mortality.
		Continu	ied on next pa	nge

Study Citation: Health You-xin, Z.Q. (2010). Toxic encephalopathy induced by occupational exposure to 1,2-dichloroethane and toxicological effect on animal model. :89-93.

ealth Mortality; Mortality;

**Outcome(s):** 

**Reported Health** 

Mortality: mortality; Mortality: mortality;

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) varying concentrations

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4492125

Domain	Metric	Rating	Comments
Metri	c 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
Metri	c 20: Negative Control Response	High	All Outcomes: A negative control group was adequate.
Domain 6: Confounding / Varia	ble Control		
Metri	c 21: Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is respiratory irritant and respiratory rates were not reported.
Metri	c 22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metri	c 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was adequately reported.
Metri	c 24: Reporting of Data	High	All Outcomes: Data were reported adequately.

# **Overall Quality Determination**

# Medium

**Study Citation:** 

You-xin, Z.Q. (2010). Toxic encephalopathy induced by occupational exposure to 1,2-dichloroethane and toxicological effect on animal model. :89-93.

Health Neurological/Behavioral; Neurological/Behavioral;

**Outcome(s):** 

Reported Health

Neurological/Behavioral: Behavior Histology and electron microscopy on brain; water content of cortex and medulla; Neurological/Behavioral: Behavior

HERO ID: 4492125 Table: 2 of 2

Effect(s): Histology and electron microscopy on brain; water content of cortex and medulla;

**Duration:** Acute (less than or equal to 24 hr) varying concentrations

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4492125

HERU ID:	4492123			
Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	Neurological/Behavioral: Test substance was identified as 1,2-dichloroethane; Neurological/Behavioral: Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was not reported. Batch or lot number was not reported.
	Metric 3:	Test Substance Purity	Low	All Outcomes: Purity of test substance was not reported.
Domain 2: Test Design				
20 1000 2 001g.	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A negative control group was sham-treated.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Study reports that animals were randomly allocated into groups.
Domain 3: Exposure C	haracterization			
Domain 3. Exposure C	Metric 7:	Preparation and Storage of Test	Low	All Outcomes: Preparation and storage were not adequately described given the volatil-
	metric 7.	Substance	Low	ity of the test substance.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Test substance was delivered consistently across study groups.
		Administration	υ	, , , , ,
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were reported and appropriate for this study type.
	Metric 11:	Number of Exposure Groups and	Medium	All Outcomes: Number of exposure groups/spacing were adequate.
		Dose/Concentration Spacing		
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The number of air changes/hour were not reported.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age of animals was not reported.
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were adequately reported.
		Husbandry Conditions	υ	
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was acceptable.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Details regarding sampling of outcomes were not adequately reported.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	All Outcomes: A negative control group was adequate.

1,1-Dichloroethane

## ... continued from previous page

Study Citation: Health You-xin, Z.Q. (2010). Toxic encephalopathy induced by occupational exposure to 1,2-dichloroethane and toxicological effect on animal model. :89-93.

HERO ID: 4492125 Table: 2 of 2

Neurological/Behavioral; Neurological/Behavioral;

Outcome(s):

Reported Health Effect(s):

Neurological/Behavioral: Behavior Histology and electron microscopy on brain; water content of cortex and medulla; Neurological/Behavioral: Behavior

Histology and electron microscopy on brain; water content of cortex and medulla;

**Duration:** Acute (less than or equal to 24 hr) varying concentrations

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4492125

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variab	ole Control		
Metric	21: Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is respiratory irritant and respiratory rates were not reported.
Metric	22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric	23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was adequately reported.
Metric	24: Reporting of Data	Low	All Outcomes: Data not presented completely, findings in all study groups were not adequately reported.

# **Overall Quality Determination**

# Medium

HERO ID: 734177 Table: 1 of 1

Study Citation: Health Outcome(s):	encephalopa			Liang, Y.X. (2011). Establishment of a poisoned animal model of toxic pathology and Pharmacology 24(1 Suppl):79S-83S.	
Reported Health Effect(s):  Duration: Chemical: HERO ID:	Neurological/Behavioral: Brain and neural cell morphology and structure evaluated using histopathology (H&E, or Hematoxylin and Eosin) and transmission electron microscopy (TEM); water content of brain tissues (cerebral cortex and medulla), which was calculated by subtracting the dry weight from the wet weight of the cortex and medulla samples.; Neurological/Behavioral: Brain and neural cell morphology and structure evaluated using histopathology (H&E, or Hematoxylin and Eosin) and transmission electron microscopy (TEM); water content of brain tissues (cerebral cortex and medulla), which was calculated by subtracting the dry weight from the wet weight of the cortex and medulla samples.; Acute (less than or equal to 24 hr) 6 Spraque-Dawley rats/sex tested (dose effects) 0, 2.5, 5, 10g/cubic m for 6hours; 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 734177				
Domain		Metric	Rating	Comments	
Domain 1: Test Substan	Metric 1:	Test Substance Identity	High	All Outcomes: Rated by authors stating full chemical name. No other identifying information of test substance, e.g., CAS#.	
	Metric 2:	Test Substance Source	Low	All Outcomes: The source was not reported and the test substance was not analytically verified by the performing laboratory. Methods did not discuss test substance other than in describing animal dose levels.	
	Metric 3:	Test Substance Purity	Low	All Outcomes: Neither purity nor grade of test substance were reported. Methods did not discuss test substance other than in describing animal dose levels.	
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	Low	Neurological/Behavioral: No lethality to determine LC- or LD50, reported in this study since animals were sacrificed no later than following 6 hours of test substance exposure. Thus this metric is applicable to this study requiring a negative concurrently run vehicle control. No information about the 'control' in this study, whether it included a vehicle was reported. Without more information, unclear if the negative control was concurrently run. The reported values for both cortex and medulla are identical for the control groups (74.22 +/- 1.77; row 1 of Tables 1 and 2). Assume it was concurrent for this dose-dependent test which was used to determine the dose for the time-dependent study, but unknown without more information.; Neurological/Behavioral: No lethality to determine LC- or LD50, reported in this study since animals were sacrificed no later than following 12 hours of test substance exposure. Thus this metric is applicable to this study requiring a negative concurrently run vehicle control. No information about the 'control' in this study, whether it included a vehicle was reported. Without more information, unclear if the negative control was concurrently run. The reported values for both cortex and medulla are identical for the control groups (74.22 +/- 1.77; row 1 of Tables and 2). Assume it was NOT concurrent for this time-dependent test which followed the dose-dependent testing, but unknown without more information.	
	Metric 5:	Positive Controls	N/A	All Outcomes: No positive control required for this acute inhalation study or the specifi neurological endpoints evaluated.	
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Study authors stated 'animals were randomly divided' to dose groups.	

HERO ID: 734177 Table: 1 of 1

#### ... continued from previous page

Study Citation:

Zhang, Q., Niu, Q., Li, L.Y., Yang, L., Guo, X.L., Huang, J.X., Wang, L.P., Liang, Y.X. (2011). Establishment of a poisoned animal model of toxic encephalopathy induced by 1,2-dichloroethane. International Journal of Immunopathology and Pharmacology 24(1 Suppl):79S-83S.

Health

Outcome(s):

Reported Health

Neurological/Behavioral: Brain and neural cell morphology and structure evaluated using histopathology (H&E, or Hematoxylin and Eosin) and transmis-

sion electron microscopy (TEM); water content of brain tissues (cerebral cortex and medulla), which was calculated by subtracting the dry weight from the wet weight of the cortex and medulla samples.; Neurological/Behavioral: Brain and neural cell morphology and structure evaluated using histopathology (H&E, or Hematoxylin and Eosin) and transmission electron microscopy (TEM); water content of brain tissues (cerebral cortex and medulla), which was calculated by subtracting the dry weight from the wet weight of the cortex and medulla samples.;

**Duration:** Acute (less than or equal to 24 hr) 6 Spraque-Dawley rats/sex tested (dose effects) 0, 2.5, 5, 10g/cubic m for 6hours;

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 734177

Effect(s):

Domain		Metric	Rating	Comments
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation, storage and method of generation of the test substance atmosphere were not reported and lack of these details could substantially impact results. No vehicle was reported.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported. For example, no information was provided to indicate that exposure was consistently administered across groups with consistent chamber designs, number of animals/chamber, and comparable particle size characteristics. Particle size was not reported. The method of inhalation exposure was not reported, if not for the units of the doses administered (g/cubic meters). Unknown whether exposure was nose/head only or whole body.
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were not reported. Reported exposure concentrations are presumably nominal, however without more information, low confidence. No other animal observations were reported, not even clinical observations, breathing rate.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type and outcome of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and concentration spacing were explicitly justified by study authors (acute study with one or two exposure groups and exposure on one day).
	Metric 12:	Exposure Route and Method	Uninformative	All Outcomes: This study provides no description of the inhalation chamber/or inhalation method of exposure. No information on nose/head only or whole body chamber exposures.
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age is not reported, and there is insufficient reporting for the number of animals per sex in each exposure group. Animal body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Some husbandry conditions are not reported (e.g., humidity). To a lesser extent, unknown how many animals per cage.
	Metric 15:	Number of Animals per Group	Low	All Outcomes: OECD GD no 39 for acute inhalation toxicity testing states that at least 6 animals/sex should have been tested per test group. Also applicable because no point estimation or lethality was determined to narrow the scope, reduce the number of animals to be tested, nor sex-specific differences accounted for prior to main study reported by the authors.

Domain 5: Outcome Assessment

HERO ID: 734177 Table: 1 of 1

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		cont	inued from previou	s page	
Study Citation:	Zhang, Q., Niu, Q., Li, L.Y., Yang, L., Guo, X.L., Huang, J.X., Wang, L.P., Liang, Y.X. (2011). Establishment of a poisoned animal model of toxic encephalopathy induced by 1,2-dichloroethane. International Journal of Immunopathology and Pharmacology 24(1 Suppl):79S-83S. Neurological/Behavioral; Neurological/Behavioral;				
Health					
<b>Outcome</b> (s):	_	-			
Reported Health Effect(s):	sion electron microscopy (TEM); water content of brain tissues (cerebral cortex and medulla), which was calculated by subtracting the dry weight from				
	(H&E, or He	ematoxylin and Eosin) and transmission electro	n microscopy (TEM	and neural cell morphology and structure evaluated using histopathology  (); water content of brain tissues (cerebral cortex and medulla), which was	
<b>Duration:</b>		y subtracting the dry weight from the wet weigh han or equal to 24 hr) 6 Spraque-Dawley rats/so			
Chemical:		bethane- Isomer: 1,2-Dichloroethane	ex tested (dose effect	s) 0, 2.3, 3, Togewore in for onours,	
HERO ID:	734177	Schalle Isomer. 1,2 Blemeroedhane			
Domain		Metric	Rating	Comments	
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: A limited number of parameters/neurological endpoints were evaluated (parameters evaluated included water content in cortex and medulla of cerebral tissue and morphology of cerebral tissues). Authors reported some cell and structure-type specific changes, however only H&E staining was used and insufficient to make definitive conclusions, e.g., enlarged mitochondria, other specific neural cell types. Cell types were generalized a 'neural cells.' No behavioral or otherwise functional evaluations were performed, nor clinical observations.	
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were limited or not reported, and these deficiencies are likely to have a substantial impact on results.	
	Metric 18:	Sampling Adequacy	Medium	Neurological/Behavioral: Insufficient information in part due to lack of reporting for certain dose and exposure duration groups.; Neurological/Behavioral: Insufficient information in part due to lack of reporting for certain exposure duration groups.	
	Metric 19:	Blinding of Assessors	Low	All Outcomes: Histopathology is subjective, especially since no cell-type specific markers were employed in the study.	
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group were adequate.	
Domain 6: Confoundi	ing / Variable Co	ntrol			
Domain o. Comound	Metric 21:	Confounding Variables in Test Design	Low	All Outcomes: No differences explicitly reported among	
	1,100110 211	and Procedures	20	study groups. Test substance is a respiratory irritant	
		and Procedures		(https://webwiser.nlm.nih.gov/substance?substanceId=431&identifier=1,2-	
				Dichloroethane&identifierType=name&menuItemId=184&catId=242), so lack of	
				information about breathing rate and other clinical observations of the animals is potentially confounding.	
	Metric 22:	Health Outcomes Unrelated to	Medium	Neurological/Behavioral: There was no information either to support or dismiss the	
		Exposure		suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment. No individua animal data were reported. Without m ore information, attrition is unknown.; Neurological/Behavioral: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment. No individual animal data were reported. Without more information, attrition is unknown.	
		Con	tinued on next page	····	

Study Citation:	Zhang, Q., Niu, Q., Li, L.Y., Yang, L., Guo, X.L., Huang, J.X., Wang, L.P., Liang, Y.X. (2011). Establishment of a poisoned animal model of toxic encephalopathy induced by 1,2-dichloroethane. International Journal of Immunopathology and Pharmacology 24(1 Suppl):79S-83S.				
Health	Neurological/Behavioral; Neurological/Behavioral;				
Outcome(s):					
Reported Health	Neurological/Behavioral: Brain and neural cell morphology and structure evaluated using histopathology (H&E, or Hematoxylin and Eosin) and transmis-				
Effect(s):	sion electron microscopy (TEM); water content of brain tissues (cerebral cortex and medulla), which was calculated by subtracting the dry weight from the wet weight of the cortex and medulla samples.; Neurological/Behavioral: Brain and neural cell morphology and structure evaluated using histopathology (H&E, or Hematoxylin and Eosin) and transmission electron microscopy (TEM); water content of brain tissues (cerebral cortex and medulla), which was calculated by subtracting the dry weight from the wet weight of the cortex and medulla samples.; Acute (less than or equal to 24 hr) 6 Spraque-Dawley rats/sex tested (dose effects) 0, 2.5, 5, 10g/cubic m for 6hours; 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 734177				
Duration: Chemical: HERO ID:					
Domain		Metric	Rating	Comments	
	Metric 23:	Data Presentation and Analysis	High	Neurological/Behavioral: Seemed acceptable with pair-wise comparison analyses per- formed.; Neurological/Behavioral: Seemed acceptable with pair-wise comparison anal- yses were performed. As reported by study authors: "Multiple pairwise comparisons among the groups were performed using ANOVA followed by denette's post hoc test."	
	Metric 24:	Reporting of Data	Low	Neurological/Behavioral: Data for exposure-related findings were not shown for each study group (dose e.g., 2.5g/cubic meter), but results were described in the text for most exposure groups. No incidences/severity per group were provided for the cerebral histopathological findings.; Neurological/Behavioral: Data for exposure duration (time)-related findings were not shown for each study group (duration e.g., 12 hours, Table 2), and results were not described in the text for most exposure duration groups, e.g. 3 hours). No incidences/severity per group were provided for the cerebral histopatholog	

# **Overall Quality Determination**

## Uninformative

Human Health Hazard Animal Toxicology Evaluation 1,1-Dichloroethane HERO ID: 77864 Table: 1 of 1

**Study Citation:** Zhao, S.F., Zhang, X.C., Zhang, L.F., Zhou, S.S., Zhang, F., Wang, Q.F., Wang, Y.L., Bao, Y.S. (1997). The evaluation of developmental toxicity of

chemicals exposed occupationally using whole embryo culture. International Journal of Developmental Biology 41(2):275-282.

Health Reproductive/Developmental

**Outcome(s):** 

**Reported Health** Developmental

Effect(s):

**Duration:** Acute (less than or equal to 24 hr) 2 day exposure in utero

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substance	e			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-Dichloroethane; a CASRN was not provided.
	Metric 2:	Test Substance Source	Low	The test substance source was not reported, and the identity was not analytically verified by the performing laboratory.
	Metric 3:	Test Substance Purity	Low	The test substance purity was not reported.
Domain 2: Test Design				
J	Metric 4:	Negative and Vehicle Controls	Low	A negative control was included, but there were insufficient details about the control (untreated or air-only)
	Metric 5:	Positive Controls	N/A	Positive controls were not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure Cha	aracterization			
	Metric 7:	Preparation and Storage of Test	Low	There was no mention of the method and equipment used to generate the test substance.
	Metric 8:	Substance Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and the missing information is likely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Low	Exposure concentrations were reported; however, it is not specified whether these were target, nominal, or measured concentrations.
	Metric 10:	Exposure Frequency and Duration	Medium	The exposure frequency/timing (GD 7 and 8) and duration were not clearly justified by the study authors. However, the exposures appeared to induce the desired response and a dose-response was observed.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included two exposure groups and a control and spacing appeared to be appropriate to identify a dose-response.
	Metric 12:	Exposure Route and Method	Uninformative	Exposure (in utero) was appropriate, but no details or description of the inhalation chamber was provided.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Animal species, strain, source, and sex were provided. Body weights and age were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not provided.

### Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

Study Citation: Zhao, S.F., Zhang, X.C., Zhang, L.F., Zhou, S.S., Zhang, F., Wang, Q.F., Wang, Y.L., Bao, Y.S. (1997). The evaluation of developmental toxicity of

chemicals exposed occupationally using whole embryo culture. International Journal of Developmental Biology 41(2):275-282.

Health Reproductive/Developmental

**Outcome(s):** 

Reported Health

**Health** Developmental

**Effect(s):** 

**Duration:** Acute (less than or equal to 24 hr) 2 day exposure in utero

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 77864

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	The number of Dams exposed was not reported; 12-17 embryos/group were sampled for explant cultures. It is unclear if these were all of the embryos evaluated or just those that were sampled.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology appeared to be sensitive for the outcome(s) of interest
	Metric 17:	Consistency of Outcome Assessment	High	Based on the information provided, there is no indication that there were any inconsis- tencies in outcome assessment across groups
	Metric 18:	Sampling Adequacy	High	The sampling appeared to be adequate and was sufficient for the purposes of the study.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes of interest.
	Metric 20:	Negative Control Response	High	The negative control responses appeared to be normal.
Domain 6: Confoundi	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not provide any information to indicate whether there were any confounding differences between groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were adequately described and were appropriate for the dataset.
	Metric 24:	Reporting of Data	High	Data were presented quantitatively as means with measures of variance. Statistical significance was indicated.

### **Overall Quality Determination**

# Uninformative

HERO ID: 4697102 Table: 1 of 1

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Study Citation:	Zhou, X., Cao, Y., Leuze, C., Nie, B., Shan, B., Zhou, W., Cipriano, P., Xiao, B.O. (2016). Early non-invasive detection of acute 1,2-dichloroethane-induced							
Health	toxic encephalopathy in rats. In Vivo 30(6):787-793.  Neurological/Behavioral; Neurological/Behavioral;							
Outcome(s):	ne(s):  ded Health  Neurological/Behavioral: Animal behavior/activity; diffusion magnetic resonance imaging on brains, histology on brains and acute 1,2-DCE-induced							
Reported Health								
Effect(s):								
Effect(s):		luced toxicencephalopathy.;	Denavion/activit	y, diffusion magnetic resonance imaging on brains, histology on brains and acute				
Duration:	Acute (less than or equal to 24 hr) 1.5 hours							
Chemical:	•	bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	4697102							
Domain		Metric	Rating	Comments				
Domain 1: Test Substanc	e							
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.				
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was Bellancom Chemistry Co. Ltd, Beijing, China. Batch/lot number was not provided.				
	Metric 3:	Test Substance Purity	Low	All Outcomes: The purity or grade of test substance was not provided.				
Domain 2: Test Design			-					
	Metric 4:	Negative and Vehicle Controls	Low	Neurological/Behavioral: Details regarding the negative control are limited. Study states control group was placed in the chamber for 4 hours and does not report any other information. Test substance animals were exposed for 1.5 hours.; Neurological/Behavioral: Details regarding the negative control are limited. Study states control group was placed in the chamber for 4 hours and does not report any other information.				
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.				
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly divided into groups.				
Domain 3: Exposure Cha								
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored.				
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure was administered consistently across study groups.				
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Target and measured concentrations with standard deviations were reported.				
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were reported and appropriate for this study type.				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Number of concentration groups and spacing studied did not yield a full range of responses. Concentrations chosen were justified.				
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: A dynamic whole body inhalation chamber was used. The number of air changes/hour was not reported.				
Domain 4: Test Animals								
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Source and age of the animals were not reported.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not adequately reported.				
		Continu	ued on next pa	ge				
			<b>F</b>	0				

Study Citation:	Zhou, X., Cao, Y., Leuze, C., Nie, B., Shan, B., Zhou, W., Cipriano, P., Xiao, B.O. (2016). Early non-invasive detection of acute 1,2-dichloroethane-induced toxic encephalopathy in rats. In Vivo 30(6):787-793.							
Health	Neurological/Behavioral; Neurological/Behavioral;							
Outcome(s):								
Reported Health	Neurological	/Behavioral: Animal behavior/activity; dif	fusion magnetic	resonance imaging on brains, histology on brains and acute 1,2-DCE-induced				
Effect(s):	toxicencephalopathy.; Neurological/Behavioral: Animal behavior/activity; diffusion magnetic resonance imaging on brains, histology on brains and acut							
	•	luced toxicencephalopathy.;	Ĭ					
Duration:		han or equal to 24 hr) 1.5 hours						
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane						
HERO ID:	4697102							
Domain		Metric	Rating	Comments				
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed /group were appropriate for the study type (n=6).				
Domain 5: Outcome A								
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodology were appropriate.				
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome was assessed consistently across study groups.				
	Metric 18:	Sampling Adequacy	Low	All Outcomes: The number of animals evaluated/group was not reported.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.				
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.				
Domain 6: Confoundin	ng / Variable Co	ıtrol						
Domain 6: Confoundi	ng / Variable Con Metric 21:	confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.				
Domain 6: Confoundii		Confounding Variables in Test Design	Low Medium	All Outcomes: No information was provided to either to support or dismiss differences				
Domain 6: Confoundi	Metric 21:	Confounding Variables in Test Design and Procedures		reported.  All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.				
Domain 6: Confoundi	Metric 21:	Confounding Variables in Test Design and Procedures Health Outcomes Unrelated to		reported.  All Outcomes: No information was provided to either to support or dismiss differences				

Human Health Hazard Animal Toxicology Evaluation

<b>Study Citation:</b>	Brondeau, M.T., Bonnet, P., Guenier, J.P., De, C.J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters
	19(1-2):139-146.
Haalth	Hangtic/Liver (Serum enzyme activity for liver damage biomarkers, SDH, GLDH, GOT, and GPT)

**Health** Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)

Outcome(s): Reported Health

Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydroge-

**Effect(s):** nase (GLDH) and sorbitol dehydrogenase (SHD).

**Duration:** Short-term (>1-30 days) Short-term- 6 hour for 2 or 4 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Test substance was identified in nomenclature as 1,2-dichloroethane; no CASRN.
Metric 2:	Test Substance Source	Low	The source of the test substance was Merck. Batch/lot numbers were not provided. Covers the lack of test substance identity in Metric 1 that did not report CASRN or chemical structure without double counting quality metrics.
Metric 3:	Test Substance Purity	High	The purity of the test substance was reported as $>99.0\%$ .
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Negative controls were exposed to clean filtered air.
Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
Metric 6:	Randomized Allocation of Animals	Low	The study did not report if/how animals were allocated.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage are not adequately described given the volatility of the test substance.
Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure were limited; however, this is unlikely to substantially impact results.
Metric 9:	Reporting of Doses/Concentrations	Medium	Target concentrations were not reported. Chemical concentration levels are means of 3-12 samples or more with continuous monitoring, with a coefficient of variation of < 13%.
Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate. 6 hour exposure (2 or 4 days).
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose group studied, based off of the lowest level of exposure that elicited significant difference (in 4 biochemical parameters, serum enzyme activity for biomarkers of liver damage) after 4 hour exposure.
Metric 12:	Exposure Route and Method	Low	Dynamic whole body inhalation chambers were used with adjustable air flows of air (10-12 m3/hr). Unknown distribution of test substance in the whole body inhalation chamber, since not reported, despite describing sampling methods. Uncertainty in parameters related to using the whole body inhalation chamber, like the number of air changes (minimum of 10/hr being required), and weather the cages were big enough for the rats and unknown how the rats were caged, possibly with more than one rat per cage.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Medium	Age of rats and individual body weights at study initiation were not reported.

Study Citation:	Brondeau, M.T., Bonnet, P., Guenier, J.P., De, C.J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.
Health	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Outcome(s):	
Reported Health	Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydroge-
Effect(s):	nase (GLDH) and sorbitol dehydrogenase (SHD).
<b>Duration:</b>	Short-term (>1-30 days) Short-term- 6 hour for 2 or 4 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200247

HERO ID:	200247			
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	No husbandry conditions were not reported, except that food and water were not available during exposure
	Metric 15:	Number of Animals per Group	Low	The number of animals treated per group was not reported/uncertain.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	Histology and organ weight was not assessed (only serum chemistry).
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding outcome assessment were limited. This is especially uncertain given the only measurements made were serum chemistry with no contextualization from body weights, liver weight, liver histology. The study authors did report that "The choice of seric parameters and sampling time was the result of preliminary experiments conducted to point out the best experimental conditions and not reported here." However, there was no reference or information provided on those parameters, which leaves uncertainty in outcome assessment consistency.
	Metric 18:	Sampling Adequacy	Low	Number of samples were variable with no accounting for how many samples comprised a specific dose or duration. Authors stating, "Exposure concentrations are the mean of 3-12 samples, or more when continuous monitoring, with a coefficient of variation of < 13% (Figure 1)." Uncertainty and only 3 samples seem insufficient.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary in this study.
	Metric 20:	Negative Control Response	Low	The biological response of the negative control responses were not shown. Data are presented as test/control means values. Can not determine if response was appropriate. The study used a manufacturer kit to measure serum enzyme activity for liver damage biomarkers. The authors stated, 'diagnostic kits purchased from Boehringer Mannheim, France,' and "Quality controls were systematically performed (Precinorm E and S, Boehringer)."
Damaia (c. Canfana	4: / 37: -b-1- C-			
Domain 6: Confound	ding / Variable Co Metric 21:	Confounding Variables in Test Design and Procedures	Low	Study did not report all information to determine confounding, reported information did not identify differences.1,2-dichloroethane is a respiratory irritant and toxicant, without respiration rate information nor other individual animal information, e.g., body weights, food and water consumption, a low confidence level is most appropriate.(EPA) https://www.epa.gov/sites/default/files/2016-09/documents/ethylene-dichloride.pdf(NJ DEH) https://nj.gov/health/eoh/rtkweb/documents/fs/0652.pdf
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed (Student's t-test).
	Metric 24:	Reporting of Data	Medium	Exposure related to stated outcomes of interest were not completely reported for this duration. Controls were only presented in a ration with treated (Figure 1).

Continued on next page ...

HERO ID: 200247 Table: 1 of 1

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

... continued from previous page

Study Citation: Brondeau, M.T., Bonnet, P., Guenier, J.P., De, C.J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters

19(1-2):139-146.

**Health** Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)

**Outcome(s):** 

Reported Health Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydroge-

**Effect(s):** nase (GLDH) and sorbitol dehydrogenase (SHD).

**Duration:** Short-term (>1-30 days) Short-term- 6 hour for 2 or 4 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200247

Domain Metric Rating Comments

Overall Quality Determination Medium

**Study Citation:** Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology

Journal 3:39-46. Nutritional/Metabolic Health

**Outcome(s):** 

**Reported Health** 

Body weight gain

Effect(s):

Short-term (>1-30 days) 5 day- reprod **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric	1: Test Substance Identity	High	Test substance was identified as 1,2-dichloroethylene (CAS No 107-06-2).
Metric	2: Test Substance Source	Low	The source of the test substance was Sigma-Aldrich (ST. Louis, Mo). Batch/lot number was not provided.
Metric	3: Test Substance Purity	High	Test substance was reported as 99.8% pure.
Domain 2: Test Design			
Metric	4: Negative and Vehicle Controls	High	The negative control group received the vehicle.
Metric		N/A	Positive control was not required in this study.
Metric	6: Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
Domain 3: Exposure Characteriz	ation		
Metric		Low	Storage conditions were not adequately described given the volatility of the test substance.
Metric		High	Test substance was administered consistently across study groups.
Metric	9: Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity.
Metric	10: Exposure Frequency and Duration	High	Exposure frequency/duration were appropriate for the study outcome (5 consecutive days).
Metric	11: Number of Exposure Groups ar Dose/Concentration Spacing	nd High	The number of dose groups was adequate and justified based on LD50.
Metric		High	Route of exposure (i.p. injection) was adequate.
Domain 4: Test Animals			
Metric	13: Test Animal Characteristics	Medium	Starting body weights were not reported.
Metric			Water availability was not reported.
Metric		Medium	The number of animals exposed /group were reported and appropriate for the study type.
Domain 5: Outcome Assessment			
Metric	16: Outcome Assessment Methodology	High	Outcome assessment and methodology were appropriate.
Metric		Medium	There was no information provided as to when or how often body weight was assessed.  This is unlikely to substantially impact results.
	18: Sampling Adequacy		

Study Citation: Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology

Journal 3:39-46. Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weight gain

Effect(s): Duration:

Health

Short-term (>1-30 days) 5 day- reprod

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5437237

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	Low	Negative control data was not reported.
Domain 6: Confounding	_			
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Study reported no change in body weight gain from control and mice maintained a healthy normal appearance.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided on infections. Animals appeared healthy. One mouse in mid dose range died 13 weeks post-treatment of undetermined cause.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	High	In results study states exposure did not effect body weight gain through out exposure or study periods

# Overall Quality Determination High

HERO ID: 5437237 Table: 2 of 4

Study Citation:

Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology Journal 3:39-46.
Renal/Kidney; Hepatic/Liver; Neurological/Behavioral;

Reported Health
Effect(s):

Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology Journal 3:39-46.
Renal/Kidney; Hepatic/Liver; Neurological/Behavioral: Gross examination of brain;

**Duration:** Short-term (>1-30 days) 5 day- reprod

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5437237

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Renal/Kidney: Test substance was identified as 1,2-dichloroethylene (CAS No 107-06-2).; Hepatic/Liver: Test substance was identified as 1,2-dichloroethylene (CAS No 107-06-2); Neurological/Behavioral: Test substance was identified as 1,2-dichloroethylene (CAS No 107-06-2).
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was Sigma-Aldrich (ST. Louis, Mo). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was reported as 99.8% pure.
Domain 2: Test Design	σn			
2. 1000 2.01	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The negative control group received the vehicle.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Study does not report how animals were allocated.
Domain 3: Exposure	Characterization			
<b>,</b>	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Storage conditions were not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Test substance was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Renal/Kidney: Administered doses were reported without ambiguity.; Hepatic/Liver: Administered doses were reported without ambiguity.; Neurological/Behavioral: Administered doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency/duration were appropriate for the study outcome (5 consecutive days).
	Metric 11:	Number of Exposure Groups and	High	All Outcomes: The number of dose groups was adequate and justified based on LD50.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	All Outcomes: Route of exposure (i.p. injection) was adequate.
Domain 4: Test Anin	nals			
Zomani ii Teot I iiiii	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Water availability was not reported.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed /group were reported and appropriate for the study type.

### Domain 5: Outcome Assessment

### Continued on next page ...

# Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

**Study Citation:** Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology Journal 3:39-46.

Renal/Kidney; Hepatic/Liver; Neurological/Behavioral; Health

**Outcome(s):** 

**Reported Health** Renal/Kidney: Gross examination of kidney; Hepatic/Liver: Gross examination of liver; Neurological/Behavioral: Gross examination of brain;

Effect(s):

**Duration:** Short-term (>1-30 days) 5 day- reprod

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5437237

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: Only gross examination on organ was done.
	Metric 17:	Consistency of Outcome Assessment	Medium	Renal/Kidney: There was limited information provided on outcome assessment protocol (gross evaluation). This is unlikely to have a substantial impact on results; Hepatic/Liver: Details were lacking regarding outcome assessment protocol. It is unlikely to have substantial impact on results.; Neurological/Behavioral: There was limited information provided on outcome assessment protocol (gross examination). This is unlikely to substantially impact results.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: It is not clear how many animals were evaluated.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	Low	All Outcomes: Negative control data was not reported.
Domain 6: Confoundin	g / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: Study reported no change in body weight gain from control and mice maintained a healthy normal appearance.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided on infections. Animals appeared healthy.  One mouse in mid dose range died 13 weeks post-treatment of undetermined cause.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistics was not necessary given no effects were observed.
	Metric 24:	Reporting of Data	High	All Outcomes: Negative results are reported in the results.

# **Overall Quality Determination**

# Medium

HERO ID: 5437237 Table: 3 of 4

**Study Citation:** Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology

Journal 3:39-46. Reproductive/Developmental Health

**Outcome(s):** 

Reported Health

Male fertility, histopathology of testis

Effect(s): **Duration:** 

Short-term (>1-30 days) 5 day- reprod

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

Domain		Metric	Rating	Comments
Domain 1: Test Substa				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethylene (CAS No 107-06-2).
	Metric 2:	Test Substance Source	Low	The source of the test substance was Sigma-Aldrich (ST. Louis, Mo). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	Test substance was reported as 99.8% pure.
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	High	The negative control group received the vehicle.
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
Domain 3: Exposure (	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Storage conditions were not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency/duration were appropriate for the study outcome (5 consecutive days).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	There were minor limitations with doses groups (a NOAEL was not obtained).
	Metric 12:	Exposure Route and Method	High	Route of exposure (i.p. injection) was adequate.
Domain 4: Test Anima	ils			
Domain 1. Test mini	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Water availability was not reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Medium	The number of animals exposed /group were reported and appropriate for the study type
		Ι Ε		I U I I II I
Domain 5: Outcome A				
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment and methodology were appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	Details of outcome assessment protocol adequate.
	Metric 18:	Sampling Adequacy	High	There was adequate sampling for the outcomes of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 5437237 Table: 3 of 4

### ... continued from previous page

**Study Citation:** Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology

Journal 3:39-46. Reproductive/Developmental Health

**Outcome(s):** 

**Reported Health** 

Male fertility, histopathology of testis

Effect(s): **Duration:** 

Short-term (>1-30 days) 5 day- reprod

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5437237

Domain		Metric	Rating	Comments
Domain 6: Confound	ing / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Study did not report food/water consumption but did report no change in body weight gain from control and mice maintained a healthy normal appearance.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided on infections. Animals appeared healthy. One mouse in mid dose range died 13 weeks post-treatment of undetermined cause.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	Low	Due to laboratory processing error, the excised testes from the 20 and 40 mg/kg dose mice were destroyed and unavailable for histological analyses.

# **Overall Quality Determination**

# High

HERO ID: 5437237 Table: 4 of 4

**Study Citation:** Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology

Journal 3:39-46. Reproductive/Developmental Health

**Outcome(s):** 

Reported Health

Male fertility, histopathology of testis

Effect(s): **Duration:** 

Short-term (>1-30 days) 5 day- time course testis path

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

	Metric	Rating	Comments
e			
Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethylene (CAS No 107-06-2).
Metric 2:	Test Substance Source	Low	The source of the test substance was Sigma-Aldrich (ST. Louis, Mo). Batch/lot number was not provided.
Metric 3:	Test Substance Purity	High	Test substance was reported as 99.8% pure.
Metric 4:	Negative and Vehicle Controls	High	The negative control group received the vehicle.
Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
Metric 6:	Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
racterization			
Metric 7:	Preparation and Storage of Test Substance	Low	Storage conditions were not adequately described given the volatility of the test substance.
Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups.
Metric 9:	Administration Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity.
Metric 10:	Exposure Frequency and Duration	High	Exposure frequency/duration were appropriate for the study outcome (5 consecutive days).
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only one dose was studied for time-course pathology. Response were seen in outcome of interest, but more doses would be helpful to understand dose effects.
Metric 12:	Exposure Route and Method	High	Route of exposure (i.p. injection) was adequate.
Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
Metric 14:	Adequacy and Consistency of Animal	Medium	Water availability was not reported.
Matria 15.		Madium	
Metric 13:	Number of Allimais per Group	Medium	The number of animals exposed /group were reported and appropriate for the study type.
essment			
Metric 16:	Outcome Assessment Methodology	High	Outcome assessment and methodology were appropriate.
Metric 17:	Consistency of Outcome Assessment	High	Details regarding testicular pathology scoring were adequate.
Metric 18:	Sampling Adequacy	Low	It is not clear how many animals were evaluated.
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
1	Metric 1: Metric 2: Metric 3:  Metric 4: Metric 5: Metric 6:  Metric 6:  Metric 8: Metric 9: Metric 10: Metric 11: Metric 12:  Metric 12:  Metric 13: Metric 14: Metric 15:  Metric 15:	Metric 1: Test Substance Identity Metric 2: Test Substance Source  Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 13: Test Animal Characteristics Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Metric 15: Number of Animals per Group  messment Metric 16: Outcome Assessment Methodology Metric 17: Consistency of Outcome Assessment Metric 18: Sampling Adequacy	Metric 1: Test Substance Identity High Metric 2: Test Substance Source Low  Metric 3: Test Substance Purity High  Metric 4: Negative and Vehicle Controls N/A Metric 5: Positive Controls N/A Metric 6: Randomized Allocation of Animals Low  Metric 7: Preparation and Storage of Test Low Substance Consistency of Exposure High Administration Metric 9: Reporting of Doses/Concentrations High Metric 10: Exposure Frequency and Duration High Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method High  Metric 13: Test Animal Characteristics Medium Husbandry Conditions Metric 14: Adequacy and Consistency of Animal Medium Husbandry Conditions Number of Animals per Group Medium  Metric 15: Number of Animals per Group Medium Metric 16: Outcome Assessment Methodology High Metric 17: Consistency of Outcome Assessment High Metric 18: Sampling Adequacy Low

Human Health Hazard Animal Toxicology Evaluation HERO ID: 5437237 Table: 4 of 4

### ... continued from previous page

**Study Citation:** Daigle, J.H., Cole, D.N., Carlson, J., Lee, W.R., Wilson, V.L. (2009). Ethylene Dichloride Disruption of Fertility in Male Mice. The Open Toxicology

Journal 3:39-46. Reproductive/Developmental Health

**Outcome(s):** 

**Reported Health** 

Male fertility, histopathology of testis

Effect(s):

**Duration:** Short-term (>1-30 days) 5 day- time course testis path Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5437237

Domain		Metric	Rating	Comments
Domain 6: Confoundi	ng / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding for the time course study. Reported information did not identify differences between the groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided on infections. Animals appeared healthy. One mouse in mid dose range died 13 weeks post-treatment of undetermined cause.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	Medium	Not all time course data was presented adequately

High

# **Overall Quality Determination**

Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley

HERO ID: 62965 Table: 1 of 4

**Study Citation:** 

Health Outcome(s): Reported Health Effect(s):  Duration: Chemical: HERO ID:	rats. Drug and Chemical Toxicology 17(4):463-477. Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/Hematological; Lung/Respiratory; Neurological/Behavioral; Nutritional/Metabolic; Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Missing 'other' target organ (Adrenal glands) pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Mortality: Mortality: Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Reproductive/Developmental: Organ weight (ovariestestes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus) gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Lung/Respiratory: Organ weight (lungs), grosn necropsy (lungs), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Lung/Respiratory: Organ weight (brain), grosn necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption; Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 62965						
Domain		Metric	Rating	Comments			
Domain 1: Test Substar	nce						
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as "1,2-dichloroethane" and synonym "ethylene dichloride." The CASRN was listed as "100706-2" instead of 107-06-2, but this is assumed to be a typo.			
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from a commercial supplier.			
	Metric 3:	Test Substance Purity	Medium	All Outcomes: It was noted that the purity of the test substance was verified by GCMS and no impurities were found; however, the numerical purity was not reported. Although the purity was not reported, this metric is rated as Medium because no impurities were found.			
Domain 2: Test Design							
C	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Corn oil vehicle controls were included.			
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.			
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: It was specified that animals were randomly allocated to vehicle and control groups.			
Domain 3: Exposure Cl	haracterization						
r same	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The test substance is volatile and was mixed fresh daily.			
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance administration appeared to be consistent across study groups and gavage volume was not excessive (0.1 mL/ 100g bw).			
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.			
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were appropriate for the intended purpose of the study.			

Continued on next page ...

**Study Citation:** Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477. Health Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Im-Outcome(s): mune/Hematological; Lung/Respiratory; Neurological/Behavioral; Nutritional/Metabolic; **Reported Health** Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin Effect(s): [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Mortality; Mortality; Cardiovascular: Organ weight (heart, gross necropsy (heart, aorta), histopathology (heart, aorta); Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Lung/Respiratory: Organ weight (lungs), gross necropsy (lungs), histopathology (lungs, nasal cavity/turbinates); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption; **Duration:** Short-term (>1-30 days) 10 days Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 62965

Domain		Metric	Ratin	Comments
	Metric 11:  Metric 12:	Number of Exposure Gro Dose/Concentration Spacing  Exposure Route and Method	oups and High	Renal/Kidney: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% the LD50.; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The rationale for the 90-day study was not specifically stated, but the 10-day study showed excessive mortality at the highest dose, 300 mg/kg/day, which was chosen because it was approximately 44% the LD50. The highest dose in the 90-day study was reduced in comparison (150 mg/kg/day).; Mortality: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% the LD50.; Cardiovascular: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% the LD50.; Reproductive/Developmental: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% the LD50.; Immune/Hematological: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% the LD50.; Lung/Respiratory: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% the LD50.; Neurological/Behavioral: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% the LD50.; Neurological/Behavioral: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Mediu	All Outcomes: Starting body weight was not reported, but the remaining characteristics were reported and appropriate. Animals were obtained from a commercial source.
			Continued on	next page

		contir	nued from p	previous page			
Study Citation:			ondie, L.W.	(1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley			
Health Outcome(s): Reported Health Effect(s):  Duration: Chemical:	rats. Drug and Chemical Toxicology 17(4):463-477. Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; In mune/Hematological; Lung/Respiratory; Neurological/Behavioral; Nutritional/Metabolic; Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirub [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Missing 'other' target organ (Adrenal gland pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Mortality Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Reproductive/Developmental: Organ weight (ovarie testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); In mune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Lung/Respiratory: Organ weight (lungs), gro necropsy (lungs), histopathology (lungs, nasal cavity/turbinates); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gro necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption; Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	62965						
Domain		Metric	Rating	Comments			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: It was reported that animals were housed in a temperature- and humidity-controlled room, but the temperature and humidity were not reported. Remaining animal husbandry parameters were reported and appropriate.			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: There were 10 animals/sex/group, which is considered appropriate for the 10-day study.			
Domain 5: Outcome	Assessment Metric 16:	Outcome Assessment Methodology  Conti	High	Renal/Kidney: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy, urine sampling, blood sampling after overnight fasting) were reported and appropriate for the outcome of interest.; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy after overnight fasting) were reported and appropriate for the outcome of interest.; Mortality: The assessment methodology (daily cageside observation) was reported and appropriate for the outcome of interest.; Cardiovascular: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, and gross necropsy) were reported and appropriate for the outcome of interest.; Reproductive/Developmental: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, and gross necropsy) were reported and appropriate for the outcome of interest.; Immune/Hematological: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy, and blood sampling after overnight fasting) were reported and appropriate for the outcome of interest.; Lung/Respiratory: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, and gross necropsy) were reported and appropriate for the outcome of interest.; Neurological/Behavioral: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy) were reported and appropriate for the outcome of interest.; Neurological/Behavioral: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy, and daily cageside observations) were reported and appropriate for the outcome of interest.; Body weights were determined on days 4, 8 and at necropsy. Food and water consumption were measured twice weekly.			
		Conti	naca on nex	n page			

**Study Citation:** 

Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477.

Health

Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/Hematological; Lung/Respiratory; Neurological/Behavioral; Nutritional/Metabolic;

Outcome(s): Reported Health Effect(s):

Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Mortality; Mortality; Cardiovascular: Organ weight (heart, gross necropsy (heart, aorta), histopathology (heart, aorta); Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Lung/Respiratory: Organ weight (lungs), gross necropsy (lungs), histopathology (lungs, nasal cavity/turbinates); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption;

**Duration:** Chemical: Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** Domain 62965

Metric Rating Comments

Metric 17: Consistency of Outcome Assessment High

Renal/Kidney: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially, which is standard practice.; Mortality: Outcome assessment was conducted consistently across control and treatment groups; "All rats were observed daily for physiological and behavioral responses as well as mortality."; Cardiovascular: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Reproductive/Developmental: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Immune/Hematological: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Lung/Respiratory: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Neurological/Behavioral: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice. For cageside observations, "all rats were observed daily for physiological and behavioral responses as well as mortality."; Nutritional/Metabolic: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided.

HERO ID: 62965 Table: 1 of 4

Continued on next page ...

**Study Citation:** Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477. Health Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Im-**Outcome(s):** mune/Hematological; Lung/Respiratory; Neurological/Behavioral; Nutritional/Metabolic;

**Reported Health** Effect(s):

Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Mortality; Mortality; Cardiovascular: Organ weight (heart, gross necropsy (heart, aorta), histopathology (heart, aorta); Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Lung/Respiratory: Organ weight (lungs), gross necropsy (lungs), histopathology (lungs, nasal cavity/turbinates); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain); Nutritional/Metabolic; Body weights, food consumption, water consumption;

HERO ID: 62965 Table: 1 of 4

**Duration: Chemical:** 

Short-term (>1-30 days) 10 days

**HERO ID:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

62965

Domain	Metric	Rating	Comments
Metric 18:	Sampling Adequacy	High	Renal/Kidney: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Mortality: All rats were assessed for mortality; therefore, the sampling is adequate.; Cardiovascular: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Reproductive/Developmental: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Immune/Hematological: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Neurological/Behavioral: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Neurological/Behavioral: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Nutritional/Metabolic: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.
Metric 19:	Blinding of Assessors	N/A	Renal/Kidney: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Mortality: No subjective measurements were assessed.; Cardiovascular: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Reproductive/Developmental: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Immune/Hematological: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Lung/Respiratory: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Neurological/Behavioral: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Nutritional/Metabolic: No subjective measurements were assessed. Blinding is not required for initial histopathology review.
Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were adequate.
nain 6: Confounding / Variable C	ontrol		
Metric 21:	Confounding Variables in Test Design	High	All Outcomes: The study protocol was well-described and no potentially confounding
Wicuic 21.	and Procedures	High	factors were identified.

Health
Outcome(s):
Reported Health

Effect(s):

**Study Citation:** 

Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477.

Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/Hematological; Lung/Respiratory; Neurological/Behavioral; Nutritional/Metabolic;

Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Mortality: Mortality; Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Lung/Respiratory: Organ weight (lungs), gross necropsy (lungs), histopathology (lungs, nasal cavity/turbinates); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption; Short-term (>1-30 days) 10 days

**Duration:** Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments
Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: No health outcomes unrelated to exposure were identified that could influence the assessment.
Metric 23:	Data Presentation and Analysis	High	Renal/Kidney: Statistical analysis is reported and appropriate for clinical chemistry and organ weight data. No statistical analysis was conducted on the gross necropsy, histopathology, or urinalysis data and no incidence information is provided; however, statistical analysis is not necessary because no findings were observed for these endpoints samples (negative data).; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Statistical analysis is reported and appropriate for organ weight data. No statistical analysis was conducted on the gross necropsy or histopathology data and no incidence information is provided; however, statistical analysis is not necessary because no findings were observed for these endpoints (negative data).; Mortality: Statistical analysis was not conducted on mortality data; however, incidence data is provided.; Cardiovascular: Statistical analysis is reported and appropriate for organ weight data. Statistical analysis is not necessary for gross necropsy and histopathological examination because no findings were observed for cardiac samples (negative data).; Reproductive/Developmental: Statistical analysis is reported and appropriate for organ weight data. Statistical analysis is not necessary for gross necropsy and histopathological examination because no findings were observed for reproductive organ samples (negative data).; Immune/Hematological: Statistical analysis is reported and appropriate for hematology, clinical chemistry, and organ weight data. Statistical analysis is not necessary for gross necropsy or histopathological examination data because no findings were observed for these assays (negative data).; Lung/Respiratory: Statistical analysis is reported and appropriate for organ weight data. Statistical analysis is not necessary for gross necropsy and histopathological examination because no findings were observed for lung/respiratory organ samples (negative data).; Neurological/Behavioral: Statistical analysis is reported and appropriate for organ weight d

HERO ID: 62965 Table: 1 of 4

### ... continued from previous page

rats. Drug and Chemical Toxicology 17(4):463-477 Renal/Kidney; Missing 'other' target organ (Adr mune/Hematological; Lung/Respiratory; Neurological Renal/Kidney: Urinalysis (pH, protein, glucose, bit [90-day only]), organ weight (kidneys), gross necropancreas, parathyroid): Organ weights (adrenals), g Cardiovascular: Organ weight (heart), gross necroptestes), gross necropsy (gonads), histopathology (gmune/Hematological: Hematology (WBC, RBC, Higgross necropsy (spleen, thymus), histopathology (sp	enal glands, pa cal/Behavioral; cirubin, urobilin psy (kidneys), h ross necropsy (a osy (heart, aorta onads, seminal gb, Hct, platelet	ncreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Im Nutritional/Metabolic; ogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin istopathology (kidneys, urinary bladder); Missing 'other' target organ (Adrenal glands adrenal glands), histopathology (adrenals, pancreas, parathyroid); Mortality: Mortality o), histopathology (heart, aorta); Reproductive/Developmental: Organ weight (ovaries vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Imcount [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus)				
Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477.  Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/Hematological; Lung/Respiratory; Neurological/Behavioral; Nutritional/Metabolic;  Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Mortality; Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Lung/Respiratory: Organ weight (brain), gross necropsy (brain), histopathology (lungs, nasal cavity/turbinates); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption; Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
Metric  Metric 24: Reporting of Data	Rating High	Comments  Renal/Kidney: All data were reported adequately. Negative findings were reported qualitatively or quantitatively.; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Negative data is adequately presented qualitatively (gross pathology, histopathology) or quantitatively (adrenal weight); Mortality: Mortality incidence data was provided.; Cardiovascular: Negative findings were reported qualitatively (gross pathology & histopathology) or quantitatively (organ weight).; Reproductive/Developmental: Negative findings were reported qualitatively (gross pathology, histopathology) or quantitatively (testes, ovary weight).; Immune/Hematological: All data were reported adequately. Negative findings were reported qualitatively (gross pathology, histopathology, hematology) or quantitatively (organ weight).; Lung/Respiratory: Negative findings were reported qualitatively (gross pathology) or quantitatively (organ weight).; Neurological/Behavioral: Negative findings were reported qualitatively (gross pathology) or quantitatively (brain weight).; Nutritional/Metabolic: All data were reported adequately. Negative findings were reported qualitatively (food and water consumption) or quantitatively (body				
	Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 62965	Short-term (>1-30 days) 10 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 62965  Metric Rating Metric 24: Reporting of Data High				

HERO ID: 62965 Table: 2 of 4

**Study Citation:** Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477. Health Hepatic/Liver Outcome(s): Reported Health Clinical chemistry (ALP, AST, ALT, cholesterol [10-day only]), organ weight (liver), gross necropsy (liver), histopathology (liver) Effect(s): **Duration:** Short-term (>1-30 days) 10 days Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 62965 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High The test substance was identified definitively as "1,2-dichloroethane" and synonym "ethylene dichloride." The CASRN was listed as "100706-2" instead of 107-06-2, but this is assumed to be a typo. Metric 2: Test Substance Source High The test substance was obtained from a commercial supplier. Metric 3: Test Substance Purity Medium It was noted that the purity of the test substance was verified by GCMS and no impurities were found; however, the numerical purity was not reported. Although the purity was not reported, this metric is rated as Medium because no impurities were found. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High Corn oil vehicle controls were included. Metric 5: Positive Controls N/A Positive controls are not required for this study type. Metric 6: Randomized Allocation of Animals Medium It was specified that animals were randomly allocated to vehicle and control groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test High The test substance is volatile and was mixed fresh daily. Substance Metric 8: Consistency of Exposure High Test substance administration appeared to be consistent across study groups and gavage volume was not excessive (0.1 mL/ 100g bw). Administration Reporting of Doses/Concentrations Metric 9: High Doses were reported without ambiguity. Metric 10: **Exposure Frequency and Duration** High The exposure frequency and duration were appropriate for the intended purpose of the study. Number of Exposure Groups and Metric 11: High The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% Dose/Concentration Spacing the LD50. Metric 12: Exposure Route and Method High The oral route was appropriate for the test substance and study type. Domain 4: Test Animals Metric 13: **Test Animal Characteristics** Medium Starting body weight was not reported, but the remaining characteristics were reported and appropriate. Animals were obtained from a commercial source. Metric 14: Adequacy and Consistency of Animal Medium It was reported that animals were housed in a temperature- and humidity-controlled room, but the temperature and humidity were not reported. Remaining animal husbandry **Husbandry Conditions** parameters were reported and appropriate. Metric 15: Number of Animals per Group Medium There were 10 animals/sex/group, which is considered appropriate for the 10-day study. Domain 5: Outcome Assessment Continued on next page ...

		···contin	ucu mom p	revious page				
Study Citation:	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawler and Chemical Toxicology 17(4):463-477.							
Health	Hepatic/Liver							
Outcome(s):								
Reported Health Effect(s):	Clinical chemistry (ALP, AST, ALT, cholesterol [10-day only]), organ weight (liver), gross necropsy (liver), histopathology (liver)							
Duration:	Short-term (>1-30 days) 10 days							
Chemical:	,	pethane- Isomer: 1,2-Dichloroethane						
HERO ID:	62965							
Domain		Metric	Rating	Comments				
	Metric 16:	Outcome Assessment Methodology	High	The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy, and blood sampling after overnight fasting) were reported and appropriate for the outcome of interest.				
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.				
	Metric 18:	Sampling Adequacy	High	All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.				
	Metric 19:	Blinding of Assessors	N/A	No subjective measurements were assessed. Blinding is not required for initial histopathology review.				
	Metric 20:	Negative Control Response	High	The negative control responses were adequate.				
Domain 6: Confoundi	ng / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	High	The study protocol was well-described and no potentially confounding factors were identified.				
	Metric 22:	Health Outcomes Unrelated to Exposure	High	No health outcomes unrelated to exposure were identified that could influence the assessment.				
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis is reported and appropriate for clinical chemistry and organ weight data. No statistical analysis was conducted on the gross necropsy and histopathology data and no incidence information is provided; however, statistical analysis is not necessary because the study focused on pathology findings.				
	Metric 24:	Reporting of Data	Medium	Negative findings were reported qualitatively (gross pathology, histopathology, clinical chemistry) or quantitatively (relative liver weight). Study authors report one clinical chemistry parameter to be significantly different from controls (males at 100 mg/kg had increased serum cholesterol levels), and this was reported as "data not shown." The magnitude of the effect was not described.				

<b>Study Citation:</b>	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley
	rats. Drug and Chemical Toxicology 17(4):463-477.
Health	Ocular/Sensory; Thyroid; Musculoskeletal; Skin/Connective Tissue;
Outcome(s):	
Deported Health	Ocular/Sansory, Onbthalmoscopic avamination (included in 90 day study only) historythology (Zymbal's gland); Thyroid; Historythology (thyroid);

Reported Health

Ocular/Sensory: Ophthalmoscopic examination (included in 90-day study only), histopathology (Zymbal's gland); Thyroid: Histopathology (thyroid);

**Effect(s):** Musculoskeletal: Histopathology (thigh muscle, sternebrae); Skin/Connective Tissue: Histopathology (skin);

Short-term (>1-30 days) 10 days **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as "1,2-dichloroethane" and synonym "ethylene dichloride." The CASRN was listed as "100706-2" instead of 107-06-2, but this is assumed to be a typo.
Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from a commercial supplier.
Metric 3:	Test Substance Purity	Medium	All Outcomes: It was noted that the purity of the test substance was verified by GCMS and no impurities were found; however, the numerical purity was not reported. Although the purity was not reported, this metric is rated as Medium because no impurities were found.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Corn oil vehicle controls were included.
Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: It was specified that animals were randomly allocated to vehicle and control groups.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The test substance is volatile and was mixed fresh daily.
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance administration appeared to be consistent across study groups and gavage volume was not excessive (0.1 mL/ 100g bw).
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were appropriate for the intended purpose of the study.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The highest dose, 300 mg/kg/day, was chosen because it was approximately 44% the LD50.
Metric 12:	Exposure Route and Method	High	All Outcomes: The oral route was appropriate for the test substance and study type.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Starting body weight was not reported, but the remaining characteristics were reported and appropriate. Animals were obtained from a commercial source.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: It was reported that animals were housed in a temperature- and humidity-controlled room, but the temperature and humidity were not reported. Remaining animal husbandry parameters were reported and appropriate.

HERO ID: 62965 Table: 3 of 4

		conti	nued from p	revious page			
Study Citation:	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawle rats. Drug and Chemical Toxicology 17(4):463-477.						
Health	Ocular/Sensory; Thyroid; Musculoskeletal; Skin/Connective Tissue;						
Outcome(s):							
Reported Health	Ocular/Sensory: Ophthalmoscopic examination (included in 90-day study only), histopathology (Zymbal's gland); Thyroid: Histopathology (thyroid:						
Effect(s):	Musculoskeletal: Histopathology (thigh muscle, sternebrae); Skin/Connective Tissue: Histopathology (skin);						
Duration:		>1-30 days) 10 days					
Chemical: HERO ID:	1,1-Dichloro 62965	bethane- Isomer: 1,2-Dichloroethane					
	02903						
Domain		Metric	Rating	Comments			
	Metric 15:	Number of Animals per Group	Medium	Ocular/Sensory: There were 10 animals/sex/group, which is considered appropriate for this study type.; Thyroid: There were 10 animals/sex/group, which is considered appropriate for the 10-day study.; Musculoskeletal: There were 10 animals/sex/group, which is considered appropriate for the 10-day study.; Skin/Connective Tissue: There were 10 animals/sex/group, which is considered appropriate for the 10-day study.			
Domain 5: Outcome	Assessment						
	Metric 16:	Outcome Assessment Methodology	High	Ocular/Sensory: The assessment methodologies (histopathology conducted by a veterinary pathologist and ophthalmoscopic examination) were reported and appropriate for the outcome of interest.; Thyroid: The assessment methodology (histopathology conducted by a veterinary pathologist) was reported and appropriate for the outcome of interest.; Musculoskeletal: The assessment methodology (histopathology conducted by a veterinary pathologist) was reported and appropriate for the outcome of interest.; Skin/Connective Tissue: The assessment methodology (histopathology conducted by a veterinary pathologist) was reported and appropriate for the outcome of interest.			
	Metric 17:	Consistency of Outcome Assessment	High	Ocular/Sensory: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed for histopathology initially, which is standard practice.; Thyroid: Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially, which is standard practice.; Musculoskeletal: Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially, which is standard practice.; Skin/Connective Tissue: Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially,			

Domain 6: Confounding / Variable Control

Metric 18:

Metric 19:

Metric 20:

Sampling Adequacy

Blinding of Assessors

Negative Control Response

Metric 21: Confounding Variables in Test Design and Procedures

Metric 22: Health Outcomes Unrelated to Exposure

High All Outcomes: The study protocol was well-described and no potentially confounding factors were identified.

All Outcomes: No health outcomes unrelated to exposure were identified that could influence the assessment.

which is standard practice.

initial histopathology review.

sampling is adequate.

All Outcomes: All 10 animals/sex/group were assessed for each endpoint; therefore, the

All Outcomes: No subjective measurements were assessed. Blinding is not required for

All Outcomes: The negative control responses were adequate.

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High

N/A

High

HERO ID: 62965 Table: 3 of 4

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Study Citation: Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley

rats. Drug and Chemical Toxicology 17(4):463-477.

**Health Outcome(s):** 

Effect(s):

Ocular/Sensory; Thyroid; Musculoskeletal; Skin/Connective Tissue;

**Reported Health** 

Ocular/Sensory: Ophthalmoscopic examination (included in 90-day study only), histopathology (Zymbal's gland); Thyroid: Histopathology (thyroid);

Musculoskeletal: Histopathology (thigh muscle, sternebrae); Skin/Connective Tissue: Histopathology (skin);

**Duration:** Short-term (>1-30 days) 10 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	N/A	Ocular/Sensory: Statistical analysis is not necessary because no histopathological findings were observed for ocular/sensory organ samples (negative data).; Thyroid: Statistical analysis is not necessary because no histopathological findings were observed for thyroid samples (negative data).; Musculoskeletal: Statistical analysis is not necessary because no histopathological findings were observed for musculoskeletal samples (negative data).; Skin/Connective Tissue: Statistical analysis is not necessary because no histopathological findings were observed for skin samples (negative data).
	Metric 24:	Reporting of Data	High	All Outcomes: Negative findings were reported qualitatively.

Overall Quality Determination	High
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HERO ID: 62965 Table: 4 of 4

**Study Citation:** Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley

rats. Drug and Chemical Toxicology 17(4):463-477.

Health

Gastrointestinal

**Outcome(s): Reported Health** 

Histopathology (esophagus, stomach, duodenum, jejunum, tongue, salivary gland, ileum, colon, cecum, rectum)

Effect(s):

**Duration:** Short-term (>1-30 days) 10 days

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substanc	e			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as "1,2-dichloroethane" and synonym "ethylene dichloride." The CASRN was listed as "100706-2" instead of 107-06-2, but this is assumed to be a typo.
	Metric 2:	Test Substance Source	High	The test substance was obtained from a commercial supplier.
	Metric 3:	Test Substance Purity	Medium	It was noted that the purity of the test substance was verified by GCMS and no impurities were found; however, the numerical purity was not reported. Although the purity was not reported, this metric is rated as Medium because no impurities were found.
Domain 2: Test Design				
· ·	Metric 4:	Negative and Vehicle Controls	High	Corn oil vehicle controls were included.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	It was specified that animals were randomly allocated to vehicle and control groups.
Domain 3: Exposure Cha	racterization			
1	Metric 7:	Preparation and Storage of Test	High	The test substance is volatile and was mixed fresh daily.
	Metric 8:	Substance Consistency of Exposure Administration	High	Test substance administration appeared to be consistent across study groups and gavage volume was not excessive (0.1 mL/ 100g bw).
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for the intended purpose of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The rationale for the 90-day study was not specifically stated, but the 10-day study showed excessive mortality at the highest dose, 300 mg/kg/day, which was chosen because it was approximately 44% the LD50. The highest dose in the 90-day study was reduced in comparison (150 mg/kg/day).
	Metric 12:	Exposure Route and Method	High	The oral route was appropriate for the test substance and study type.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weight was not reported, but the remaining characteristics were reported and appropriate. Animals were obtained from a commercial source.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	It was reported that animals were housed in a temperature- and humidity-controlled room, but the temperature and humidity were not reported. Remaining animal husbandry parameters were reported and appropriate.
	Metric 15:	Number of Animals per Group	Medium	There were 10 animals/sex/group, which is considered appropriate for the 10-day study.

HERO ID: 62965 Table: 4 of 4

1,1-Dichloroethane

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Study Citation: Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley

rats. Drug and Chemical Toxicology 17(4):463-477.

Health

Gastrointestinal

**Outcome(s):** 

Reported Health Histopathology (esophagus, stomach, duodenum, jejunum, tongue, salivary gland, ileum, colon, cecum, rectum)

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 10 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62965

Domain		Metric	Rating	Comments
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The assessment methodology (histopathology conducted by a veterinary pathologist) was reported and appropriate for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially, which is standard practice.
	Metric 18:	Sampling Adequacy	High	All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.
	Metric 19:	Blinding of Assessors	N/A	No subjective measurements were assessed. Blinding is not required for initial histopathology review.
	Metric 20:	Negative Control Response	High	The negative control responses were adequate.
Domain 6: Confound	ding / Variable Co Metric 21:	ntrol Confounding Variables in Test Design and Procedures	High	The study protocol was well-described and no potentially confounding factors were identified.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	No health outcomes unrelated to exposure were identified that could influence the assessment.
	Metric 23:	Data Presentation and Analysis	Uninformative	No statistical analysis was conducted on the histopathology data and no incidence data is provided. Study authors state that the "only microscopic change consistently noted at 100 mg/kg was inflammation of the mucosal and submucosal layers of the forestomach of minimal severity." However, no statistical analysis was conducted on the histopathology data and no incidence data is provided so independent analysis cannot be performed.
	Metric 24:	Reporting of Data	Low	Data for exposure-related findings (i.e., incidence data for inflammation in the forestom- ach was not shown) were not shown for each study group, but results were described in the text.

# **Overall Quality Determination**

### Uninformative

Study Citation: Health	Dow Chemical, (2014). [Redacted] Investigation of the mode of action for 1,2-dichloroethane-induced mammary tumors in female F344/DuCrl rats. Genotoxicity (Genotoxicity)						
Outcome(s): Reported Health	Comet assay on mammary gland cells						
Effect(s):							
Duration:	Short-term (>1-30 days) at least 28 days (ranged from 28-31; sacrificed immediately after exposure on the first diestrus)						
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	10609985						
Domain		Metric	Rating	Comments			
Domain 1: Test Substan	ce						
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.			
	Metric 2:	Test Substance Source	High	The source of the test substance was identified as Fisher Scientific, Suwanee, Georgia (Lot # 125002).			
	Metric 3:	Test Substance Purity	High	Purity of the test material is listed as 99.9% per non-GLP certificate of analysis.			
Domain 2: Test Design							
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group was included (air exposed).			
	Metric 5:	Positive Controls	Medium	A concurrent positive control was included for the Comet assay.			
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were stratified by body weight and then randomly assigned to treatment groups			
	Medie o.	randomized i mocation of i minimals	Wicarain	using a computer program designed to increase the probability of uniform group mean weights.			
Domain 3: Exposure Ch	aracterization						
Domain 3. Exposure en	Metric 7:	Preparation and Storage of Test	Medium	The test substance is volatile and storge conditions were not reported. The preparation,			
	wiedle 7.	Substance	Wicdiani	method and equipment used to generate the test substance was adequately reported.			
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups.			
		Administration					
	Metric 9:	Reporting of Doses/Concentrations	High	Nominal and actual concentrations were reported and within 10%.			
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for outcomes of interest (6 hours/day; 7 days/week for 28 days).			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only one concentration level was examined and this was based on previous studies that exposed rats for 2 years (Nagano 2006). No effects were seen in this study, it is unclear if higher concentration would have resulted in positive response.			
	Metric 12:	Exposure Route and Method	Medium	A dynamic whole-body inhalation chamber was used; air changes averaged 10-15 times/hour.			
Domain 4: Test Animals	S						
	Metric 13:	Test Animal Characteristics	High	The species, strain, source, starting body weight, and age were reported.			
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were fully reported and consistent between the groups.			
		Husbandry Conditions	J				
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was appropriate (n=28).			
Domain 5: Outcome Ass	sessment						
		Contin	nued on nex	kt page			

HERO ID: 10609985 Table: 1 of 2

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		··· contin	iueu iroin p	revious page			
Study Citation: Health	Dow Chemical, (2014). [Redacted] Investigation of the mode of action for 1,2-dichloroethane-induced mammary tumors in female F344/DuCrl rats. Genotoxicity (Genotoxicity)						
Outcome(s):							
Reported Health	Comet assay	on mammary gland cells					
Effect(s):	Cornet assay on manmary grand cons						
Duration:	Short-term (	>1-30 days) at least 28 days (ranged from 3	28-31: sacrif	iced immediately after exposure on the first diestrus)			
Chemical:	Short-term (>1-30 days) at least 28 days (ranged from 28-31; sacrificed immediately after exposure on the first diestrus) 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	10609985						
iieko ib.	10007703						
Domain		Metric	Rating	Comments			
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessments methodology were appropriate for intended outcome of interest; controlled for estrous cycle by sacrificing at same point in cycle.			
	Metric 17:	Consistency of Outcome Assessment	High	Assessment protocol was reported and assessed consistently across study groups.			
	Metric 18:	Sampling Adequacy	High	Sampling was adequate and reported in results.			
	Metric 19:	Blinding of Assessors	N/A	Blinding of assessors was not necessary.			
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.			
Domain 6: Confoundi	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Food intake and body weight changes were reported. Respiratory rate was not reported. The test substance is respiratory irritant, and therefore respiratory rate should be provided to determine any confounding effects.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure. All animals were accounted for in results, and there was no indication of disease.			
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis of data was reported and appropriate.			
	Metric 24:	Reporting of Data	High	Data were fully reported for outcomes of interest. Individual animal results are reported			

# **Overall Quality Determination**

# High

Study Citation: Health	Dow Chemical, (2014). [Redacted] Investigation of the mode of action for 1,2-dichloroethane-induced mammary tumors in female F344/DuCrl rats. Nutritional/Metabolic; Mortality; Reproductive/Developmental; Clinical signs (Clinical Signs);							
<b>Outcome</b> (s):								
Reported Health Effect(s):	Nutritional/Metabolic: Body weight and food intake; Mortality: Mortality and morbididty; Reproductive/Developmental: Serum prolactin levels, mo phometry of mammary gland structure, histopathology on mammary gland, cell proliferation (Ki-57) on mammary gland cells.Non-apical: levels of reduced (GSH) and oxidized (GSSG) glutathione, DCE-glutathione conjugates S-(2-Hydroxyethyl)glutathione hydrochloride (HESG) and S,S'-Ethyleneb glutathione (EBG), DNA adducts 8-Hydroxy-2'-deoxyguanosine (8-OH dG), S-(2- guanylethyl) glutathione (GEG), and DNA damage (Comet assay) mammary tissue; Clinical signs (Clinical Signs): Cage-side and clinical observations; hands-on evaluation;							
Duration:	Short-term (>1-30 days) at least 28 days (ranged from 28-31; sacrificed immediately after exposure on the first diestrus)							
Chemical: HERO ID:	1,1-Dichloro 10609985	ethane- Isomer: 1,2-Dichloroethane						
Domain		Metric	Rating	Comments				
Domain 1: Test Substan	ice							
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.				
	Metric 2:	Test Substance Source	High	All Outcomes: The source of the test substance was identified as Fisher Scientific, Suwanee, Georgia (Lot # 125002).				
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity of the test material is listed as 99.9% per non-GLP certificate of analysis.				
Domain 2: Test Design								
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A concurrent negative control group was included (air exposed).				
	Metric 5:	Positive Controls	N/A	All Outcomes: A concurrent positive control was not needed for this study design for apical endpoints.				
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights.				
Domain 3: Exposure Ch	naracterization							
· · · · · · · · · · · · · · · · · · ·	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The test substance is volatile and storge conditions were not reported. The preparation, method and equipment used to generate the test substance was adequately reported.				
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance was administered consistently across study groups.				
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Nominal and actual concentrations were reported and within 10%.				
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were appropriate for outcomes of interest (6 hours/day; 7 days/week for 28 days).				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Only one concentration level was examined and this was based on previous studies that exposed rats for 2 years (Nagano 2006). No effects were seen in this study, it is unclear if higher concentration would have resulted in positive response.				
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: A dynamic whole-body inhalation chamber was used; air changes averaged 10-15 times/hour.				
Domain 4: Test Animal	s							
	Metric 13:	Test Animal Characteristics	High	All Outcomes: The species, strain, source, starting body weight, and age were reported.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Husbandry conditions were fully reported and consistent between the groups.				
		Contin	nued on nex	kt page				

utritional/Monometry of raced (GSH) utathione (Eammary tiss nort-term (>	etabolic; Mortality; Reproductive/Develop etabolic: Body weight and food intake; Mammary gland structure, histopathology and oxidized (GSSG) glutathione, DCE-gl BG), DNA adducts 8-Hydroxy-2'-deoxyg ue; Clinical signs (Clinical Signs): Cage-s	Mortality: Mortality: Mon mammar lutathione coguanosine (8 kide and clini	Mortality and morbididty; Reproductive/Developmental: Serum prolactin levels, morry gland, cell proliferation (Ki-57) on mammary gland cells.Non-apical: levels of reonjugates S-(2-Hydroxyethyl)glutathione hydrochloride (HESG) and S,S'-Ethylenebis B-OH dG), S-(2- guanylethyl) glutathione (GEG), and DNA damage (Comet assay) in
nometry of raced (GSH) utathione (Eammary tiss nort-term (> 1-Dichloroe 0609985	nammary gland structure, histopathology and oxidized (GSSG) glutathione, DCE-gl. (BG), DNA adducts 8-Hydroxy-2'-deoxygue; Clinical signs (Clinical Signs): Cage-s 1-30 days) at least 28 days (ranged from 2 thane- Isomer: 1,2-Dichloroethane	on mammar lutathione co guanosine (8 ide and clin	ry gland, cell proliferation (Ki-57) on mammary gland cells.Non-apical: levels of reonjugates S-(2-Hydroxyethyl)glutathione hydrochloride (HESG) and S,S'-Ethylenebis B-OH dG), S-(2- guanylethyl) glutathione (GEG), and DNA damage (Comet assay) in ical observations; hands-on evaluation;
nometry of raced (GSH) utathione (Eammary tiss nort-term (> 1-Dichloroe 0609985	nammary gland structure, histopathology and oxidized (GSSG) glutathione, DCE-gl. (BG), DNA adducts 8-Hydroxy-2'-deoxygue; Clinical signs (Clinical Signs): Cage-s 1-30 days) at least 28 days (ranged from 2 thane- Isomer: 1,2-Dichloroethane	on mammar lutathione co guanosine (8 ide and clin	ry gland, cell proliferation (Ki-57) on mammary gland cells.Non-apical: levels of reonjugates S-(2-Hydroxyethyl)glutathione hydrochloride (HESG) and S,S'-Ethylenebis B-OH dG), S-(2- guanylethyl) glutathione (GEG), and DNA damage (Comet assay) in ical observations; hands-on evaluation;
nort-term (> 1-Dichloroe 0609985	1-30 days) at least 28 days (ranged from 2 thane- Isomer: 1,2-Dichloroethane		
1-Dichloroe )609985	thane- Isomer: 1,2-Dichloroethane		
0609985	,		
letric 15:	Metric		
letric 15:		Rating	Comments
	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was appropriate (n=28).
ment letric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessments methodology were appropriate for intended outcome of interest; controlled for estrous cycle by sacrificing at same point in cycle.
letric 17:	Consistency of Outcome Assessment	High	All Outcomes: Assessment protocol was reported and assessed consistently across study groups.
letric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate and reported in results.
letric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding of assessors was not necessary.
letric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.
ariable Cont	rol		
letric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Food intake and body weight changes were reported. Respiratory rate was not reported. The test substance is respiratory irritant, and therefore respiratory rate should be provided to determine any confounding effects.
letric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure. All animals were accounted for in results, and there was no indication of disease.
letric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis of data was reported and appropriate.
letric 24:	Reporting of Data	High	All Outcomes: Data were fully reported for outcomes of interest. Individual animal results are reported.
Overall Quality Determination			
le le le	etric 17: etric 18: etric 19: etric 20: riable Cont etric 21: etric 22: etric 22:	etric 17: Consistency of Outcome Assessment etric 18: Sampling Adequacy etric 19: Blinding of Assessors etric 20: Negative Control Response  riable Control etric 21: Confounding Variables in Test Design and Procedures  etric 22: Health Outcomes Unrelated to Exposure  etric 23: Data Presentation and Analysis etric 24: Reporting of Data	etric 17: Consistency of Outcome Assessment High etric 18: Sampling Adequacy High etric 19: Blinding of Assessors N/A etric 20: Negative Control Response High etric 21: Confounding Variables in Test Design and Procedures etric 22: Health Outcomes Unrelated to Exposure etric 23: Data Presentation and Analysis High etric 24: Reporting of Data High

**Study Citation:** 

Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

Effect(s):

**Duration:** Short-term (>1-30 days) Inhalation

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	023200			
Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2 dichloroethane.
	Metric 2:	Test Substance Source	High	The source of the test substance was Occidental Chemical Corporation, Dallas, TX (batch # 303MICHIGA).
	Metric 3:	Test Substance Purity	High	Purity was 99.9%; determined by GC/thermal conductivity detection.
Domain 2: Test Desig	n			
	Metric 4:	Negative and Vehicle Controls	Uninformative	The study is unacceptable because only for the one-day exposure are the controls not exposed to the test substance (vehicle only). Therefore, there is not an unexposed control and any adverse effects on body weight due to 1,2-dichloroethnane exposure can not be determined
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	"Animals were randomly assigned to treatment groups using a computer-driven program that minimized the differences between mean body weights".
Domain 3: Exposure	Characterization			
Domain 3. Exposure	Metric 7:	Preparation and Storage of Test	High	Test substance preparation and storage was fully described.
	Metric 8:	Substance Consistency of Exposure	High	Exposures were administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity. For inhalation, nominal and actual concentration were reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for aim of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only one dose/concentration was studied. Therefore, both a NOAEL and LOAEL were not obtained. The study based the dose/concentration on previous toxicity information.
	Metric 12:	Exposure Route and Method	High	For inhalation, a nose-only chamber was used with airflow maintained at 60L/minute.
Domain 4: Test Anim	als			
20114111 11 1000 1 1111111	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported.
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.
	Metric 15:	Husbandry Conditions Number of Animals per Group	Medium	The number of animals/group was adequate for this study type (n=3).
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome methodology (Body weight) was assessed appropriately.
		Conti	nued on next pag	e

**Study Citation:** 

Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.

Health

th Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

Effect(s):

**Duration:** Short-term (>1-30 days) Inhalation

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 625286

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	High	Assessment protocol was consistent across study groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate; all animals were accounted for.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for body weight.
	Metric 20:	Negative Control Response	High	Biological response of negative control was appropriate.
Domain 6: Confounding	/ Variable Cor Metric 21:	confounding Variables in Test Design and Procedures	Low	The test substance is a respiratory irritant. The study did not report respiratory rate. Food intake was not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed, but study provided sufficient data for independent statistics.
	Metric 24:	Reporting of Data	High	Data were fully reported with individual animal data.

# **Overall Quality Determination**

# High

HERO ID: 625286 Table: 2 of 2

**Study Citation:** 

Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

Effect(s):

**Duration:** Short-term (>1-30 days) Gavage

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2 dichloroethane.
	Metric 2:	Test Substance Source	High	The source of the test substance was Occidental Chemical Corporation, Dallas, TX (batch # 303MICHIGA).
	Metric 3:	Test Substance Purity	High	Purity was 99.9%; determined by GC/thermal conductivity detection.
Di 2. T+ Di				
Domain 2: Test Design	Metric 4:	Magative and Vahiala Controls	Uninformative	
	Metric 4:	Negative and Vehicle Controls	Uninformative	The study is unacceptable because only for the one-day exposure are the controls not exposed to the test substance (vehicle only). Therefore, there is not an unexposed control and any adverse effects on body weight due to 1,2-dichloroethnane exposure can not be determined.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	"Animals were randomly assigned to treatment groups using a computer-driven program that minimized the differences between mean body weights".
Domain 3: Exposure Ch	aracterization			
Domain J. Exposure en	Metric 7:	Preparation and Storage of Test	High	Test substance preparation and storage was fully described.
		Substance	8	
	Metric 8:	Consistency of Exposure	High	Exposures were administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for aim of the study.
	Metric 11:	Number of Exposure Groups and	Medium	Only one dose/concentration was studied. Therefore, both a NOAEL and LOAEL were
		Dose/Concentration Spacing		not obtained. The study based the dose/concentration on previous toxicity information.
	Metric 12:	Exposure Route and Method	High	The route (gavage) was appropriate for test substance.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported.
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.
		Husbandry Conditions	_	
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was adequate for this study type (n=3).
Domain 5: Outcome Ass	sessment			
2 smain 5. Gutcome 7 is	Metric 16:	Outcome Assessment Methodology	High	The outcome methodology (Body weight) was assessed appropriately.
	Metric 17:	Consistency of Outcome Assessment	High	Assessment protocol was consistent across study groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate; all animals were accounted for.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for body weight.
			nued on next pag	

HERO ID: 625286 Table: 2 of 2

1,1-Dichloroethane

### ... continued from previous page

**Study Citation:** 

Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight

Effect(s): Duration:

Short-term (>1-30 days) Gavage

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 625286

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	High	Biological response of negative control was appropriate.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding. Food intake was not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed, but study provided sufficient data for independent statistics.
	Metric 24:	Reporting of Data	High	Data were fully reported with individual animal data.

# **Overall Quality Determination**

# High

Study Citation:	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.
Health	Mortality

**Outcome(s):** 

**Reported Health** Mortality

Effect(s):

**Duration:** Short-term (>1-30 days) Short-term; 2-weeks Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772372

HERO ID.	1//23/2			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was definitively identified as 1,2-dichloroethane. A CASRN was not provided.
	Metric 2:	Test Substance Source	High	The test substance was sourced from Merk, the form was specified (liquid).
	Metric 3:	Test Substance Purity	High	The test substance purity was 99%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	A concurrent olive oil vehicle control was included.
	Metric 5:	Positive Controls	N/A	Positive controls are not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report the method of animal allocation, or whether other methods of normalization were used.
Domain 3: Exposure Ch	aracterization			
2 Small St Exposure Of	Metric 7:	Preparation and Storage of Test Substance	Medium	The mg quantities of the test material for each dose group were "dissolved in 10 mL of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.
	Metric 8:	Consistency of Exposure Administration	Low	Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights ranged from 80-90g, in which case, this gavage volume would be excessive.
	Metric 9:	Reporting of Doses/Concentrations	Medium	It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.
	Metric 12:	Exposure Route and Method	High	Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.
Domain 4: Test Animals				
20	Metric 13:	Test Animal Characteristics	Medium	SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.

HERO ID: 1772372 Table: 1 of 3

		contin	ued from p	revious page
Study Citation: Health	Esch, van, G Mortality	. J., Kroes, R., Logten, van, M. J., Tonkelaa	r, den, E. M	. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.
Outcome(s): Reported Health Effect(s):	Mortality			
Duration: Chemical: HERO ID:		>1-30 days) Short-term; 2-weeks ethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry details were limited to food and water availability and the number of animals per cage (2/cage). Other details (e.g., temperature, humidity, light cycle), were not reported. Insufficient information was provided to determine whether there was consistency across groups.
	Metric 15:	Number of Animals per Group	Medium	The study used 6 male rats/group. The authors did not justify the use of males only. The number of animals/group was sufficient to allow for statistical analysis.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	The study methods did not explicitly specify that animals were observed for mortality; however, mortality results were reported. There are no concerns with the assessment of this outcome.
	Metric 17:	Consistency of Outcome Assessment	High	No methods or details of animal observation for this outcome were provided, but the data suggest that all animals were observed for this outcome.
	Metric 18:	Sampling Adequacy	High	The sampling was not explicitly stated, but it is assumed that all animals were observed for mortality since the number of animals died were reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary or required for outcomes that are either not subjective in nature, or are simple measures. Blinding is not recommended for initial histopathological examinations.
	Metric 20:	Negative Control Response	High	No deaths in the control group was specified.
Domain 6: Confoundin	ng / Variable Co	ntrol		
Domain o. Comoundin	Metric 21:	Confounding Variables in Test Design and Procedures	High	The study recorded most information to determine confounding (e.g., body weights and food intake), and there were no differences across groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods in general were described. It is unclear whether statistical analysis was applied to this outcome, but an independent analysis could be done based on the information provided.
	Metric 24:	Reporting of Data	High	Animal deaths were adequately described in the text including the time(s) of death, a

HERO ID: 1772372 Table: 2 of 3

Reported Health Body weights, growth, food intake  Effect(s):  Duration: Short-term (>1-30 days) Short-term; 2-weeks	Study Citation: Health	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Nutritional/Metabolic					
Domain   Short-term     1-30 days) Short-term; 2-weeks   1-1-10 febrorethane   1-1-10	Outcome(s): Reported Health Effect(s):	Body weight	s, growth, food intake				
Domain 1: Test Substance Metric 2: Test Substance Identity Metric 2: Test Substance Domain 2: Test Design Metric 3: Test Substance Purity Metric 5: Positive Controls Metric 6: Positive Controls Metric 6: Randomized Allocation of Animals Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Metric 12: Exposure Frequency and Method Metric 12: Exposure Route and Method Metric 12: Exposure Route and Method Metric 12: Test Animals Metric 13: Test Animal Search and the Accessing Administration Medium Animals were considered that feeding studies were recommended by FAO/WHO.  Medium Animals were considered that feeding studies were recommended by FAO/WHO.  Medium Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.  Medium Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.  Domain 4: Test Animals Metric 13: Test Animal Characteristics  Medium SPF Wistar as were used. The animal starting body weights, source, and sex were reported. A	Duration: Chemical:	1,1-Dichloro					
Domain 1: Test Substance Metric 1: Test Substance Identity Metric 2: Test Substance Identity Metric 3: Test Substance Purity High The test substance was definitively identified as 1,2-dichloroethane. A CASRN was not provided. Metric 3: Test Substance Purity High The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was sourced from Merk, the form was specified (liquid). The test substance was found to excessive of the study type. The study did not report the study type. The study did not report the method of animal allocation, or whether other methods of normalization were used. The method of animal allocation, or whether other methods of onimal allocation, or whether other methods of olive oil's however the test material for cach dose group were "dissolved in 10 mL of olive oil's however the test material was reported to be a liquid. The frequency of the study in the lack of details on storage in similary to affect results.  Metric 9: Reporting of Exposure Reporting of Doses/Concentrations Metric 9: Reporting of Do		1772372	Matric	Pating	Comments		
Metric 1: Test Substance Identity  Metric 2: Test Substance Source Metric 3: Test Substance Source Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Metric 10: Exposure Frequency and Duration Metric 12: Exposure Route and Method  Metric 13: Test Animals  Metric 13: Test Animals Metric 13: Test Animals Characteristics  Medium  SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test substance was specified of the test material for each dose group were "dissolved in 10 ml. of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.  Medium  The meg quantities of the test material for each dose group were "dissolved in 10 ml. of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.  Medium  The medium and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to that the study and the study of details on storage is unlikely to have a substance were detailed in successive.  It was not specified whether the reported doses were target on nominal. There is no indication that its gravey volume ments were conducted, but this is		ce	Wettic	Kating	Comments		
Metric 3: Test Substance Purity   High   The test substance purity was 99%	Domain 1. Test Substan		Test Substance Identity	High			
Metric 3: Test Substance Purity   High   The test substance purity was 99%		Metric 2:	Test Substance Source	High	The test substance was sourced from Merk, the form was specified (liquid).		
Metric 5: Positive Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals Low Preparation and Storage of Test Substance  Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance  Description of Animals Metric 8: Consistency of Exposure Administration Administration  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 13: Test Animals Metric 13: Test Animal Characteristics  Medium SPF Wistar rats were used. The east of one of the test material was reported to be a fiquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal.		Metric 3:	Test Substance Purity	High	The test substance purity was 99%		
Metric 5: Positive Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals Low Preparation and Storage of Test Substance  Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance  Description of Animals Metric 8: Consistency of Exposure Administration Administration  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 13: Test Animals Metric 13: Test Animal Characteristics  Medium SPF Wistar rats were used. The east of one of the test material was reported to be a fiquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium It was not specified whether the reported doses were target or nominal.	Domain 2: Test Design						
Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals Low The study did not report the method of animal allocation, or whether other methods of normalization were used.  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance  Preparation and Storage of Test Substance  Medium The mg quantities of the test material for each dose group were "dissolved in 10 mL of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.  Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Doses/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 13: Test Animals  Metric 13: Test Animals  Metric 13: Test Animal Characteristics  Medium SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.	Domain 2. Test Design	Metric 4	Negative and Vehicle Controls	High	A concurrent olive oil vehicle control was included		
Metric 6: Randomized Allocation of Animals Low The study did not report the method of animal allocation, or whether other methods of normalization were used.  Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance  Preparation and Storage of Test Substance  Medium Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 13: Test Animals  Metric 13: Test Animals  Metric 13: Test Animal Characteristics  Medium  The study did not report the method of animal allocation, or whether other methods of normalization were used.  The study did not report the method of animal allocation, or whether other methods of normalization were used.  Medium of the test material for each dose group were "dissolved in 10 mL of olive oil": however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.  Medium (Medium)  Medium National from 80-90g, in which case, this gavage volume would be excessive.  Medium Animals were dosed whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Medium Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifiedly justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  Metric 11: Number of Exposure Groups and pose-finding study included 5 exposure groups and a control. The number and spacing was appropriate.  Medium Number of Exposure Route and Method  SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was			C				
Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups Metric 12: Exposure Route and Method Metric 12: Exposure Route and Method  Metric 13: Test Animals  Metric 13: Test Animals  Medium  The mg quantities of the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.  Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights ranged from 80-90g, in which case, this gavage volume would be excessive.  Medium  Medium  Medium  Medium  Medium  Medium  Medium  Medium  Medium Stread Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.  High  Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.  SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.					* * * *		
Metric 7: Preparation and Storage of Test Substance Substance  Medium Metric 8: Consistency of Exposure Administration  Medium Metric 9: Reporting of Doses/Concentrations Medium Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 13: Test Animals  Medium  The mg quantities of the test material for each dose group were "dissolved in 10 mL of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were root specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.  Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights ranged from 80-90g, in which case, this gavage volume would be excessive.  It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.  Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics  Medium  SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.					•		
Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations  Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 13: Test Animals  Metric 14: Low Administration  Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Test Animals  Metric 13: Test Animal Characteristics  Medium SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.	Domain 3: Exposure Ch		-	Medium	olive oil"; however the test material was reported to be a liquid. The frequency of the		
Metric 9: Reporting of Doses/Concentrations Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.  Metric 10: Exposure Frequency and Duration Medium Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method High Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics Medium SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.		Metric 8:		Low	Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights		
Metric 10: Exposure Frequency and Duration  Medium Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method High Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.  Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.  Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specified by two 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.  Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specified by two 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.  This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.  Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding study included 5 exposure groups and a control. The number and spacing was appropriate.  By a support of the control of the		Metric 9:	Reporting of Doses/Concentrations	Medium	It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have		
Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 13: Test Animals  Metric 13: Test Animal Characteristics  Medium  Metric 14: Number of Exposure Groups and High This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.  High Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.  Medium SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.		Metric 10:	Exposure Frequency and Duration	Medium	Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week		
Metric 12: Exposure Route and Method  High Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics  Medium SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.		Metric 11:		High	This range-finding study included 5 exposure groups and a control. The number and		
Metric 13: Test Animal Characteristics Medium SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.		Metric 12:	Exposure Route and Method	High	ical, although, in the introduction, the authors noted that feeding studies were recom-		
Metric 13: Test Animal Characteristics Medium SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.	Domain 4: Test Animals						
Continued on next page	2550		Test Animal Characteristics	Medium	reported. Age was not specified. The test species were appropriate for the outcomes of		
- · · · · · · · · · · · · · · · · · · ·			Contin	nued on nex	t page		

		contin	ued from p	revious page			
Study Citation: Health	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Nutritional/Metabolic						
Outcome(s): Reported Health Effect(s):	Body weights, growth, food intake						
Duration: Chemical: HERO ID:		>1-30 days) Short-term; 2-weeks bethane- Isomer: 1,2-Dichloroethane					
Domain		Metric	Rating	Comments			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry details were limited to food and water availability and the number of animals per cage (2/cage). Other details (e.g., temperature, humidity, light cycle), were not reported. Insufficient information was provided to determine whether there was consistency across groups.			
	Metric 15:	Number of Animals per Group	Medium	The study used 6 male rats/group. The authors did not justify the use of males only. The number of animals/group was sufficient to allow for statistical analysis.			
Domain 5: Outcome A	ssessment						
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methods were clearly described, including the timing/frequency of measurements. The methods were sensitive to the outcomes of interest.			
	Metric 17: Metric 18:	Consistency of Outcome Assessment Sampling Adequacy	High High	Based on the information provided, animals from all groups were consistently assessed.  All of the surviving animals were sampled for the outcomes of interest.			
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary or required for outcomes that are either not subjective in nature, or are simple measures. Blinding is not recommended for initial histopathological examinations.			
	Metric 20:	Negative Control Response	High	The negative control responses were quantitatively reported and were appropriate.			
Domain 6: Confoundir	ng / Variable Co	ntrol					
2 cmain or comounding	Metric 21:	Confounding Variables in Test Design and Procedures	High	The study recorded most information to determine confounding (e.g., body weights and food intake), and there were no differences across groups.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods in general were described and were appropriate for the datasets.			
	Metric 24:	Reporting of Data	Low	Continuous data for these outcomes were reported as means without measures of variance.			
Overall Quali	ity Detern	nination	High				

HERO ID: 1772372 Table: 3 of 3

Study Citation: Health Outcome(s):		G. J., Kroes, R., Logten, van, M. J., Tonkelaa ey; Endocrine (Endocrine); Reproductive/De		. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. l; Hepatic/Liver;
Reported Health Effect(s):	(adrenals, pi atic/Liver: o	ituitary, pancreas); Reproductive/Developm organ weights; clinical chemistry (serum SC	ental: Orgai GPT and AL	ney); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology n weights (uterus, ovary, testes), histopathology (uterus, ovary, testes, prostate); Hep-Pactivity: 90-day study), BSP retention (both durations); in the liver (SGPT activity av only] and triglyceride content [both durations]); histopathology.;
Duration: Chemical: HERO ID:	Short-term (	>1-30 days) Short-term; 2-weeks bethane- Isomer: 1,2-Dichloroethane	ouviey (50 de	ay omy j and argifeeride content [com datations]), insteputationegy.,
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was definitively identified as 1,2-dichloroethane. A CASRN was not provided.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was sourced from Merk, the form was specified (liquid).
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance purity was 99%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A concurrent olive oil vehicle control was included.
	Metric 5: Metric 6:	Positive Controls Randomized Allocation of Animals	N/A Low	All Outcomes: Positive controls are not necessary for the study type.  All Outcomes: The study did not report the method of animal allocation, or whether other methods of normalization were used.
				other methods of normanization were used.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The mg quantities of the test material for each dose group were "dissolved in 10 mL of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. Since this is a short-term study, the lack of details on storage is unlikely to affect results.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights ranged from 80-90g, in which case, this gavage volume would be excessive.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on results.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Animals were dosed via gavage 5 days per week for a period of two weeks. The study authors did not specifically justify the 5-day/week dosing schedule, but the 2-week duration is acceptable for a range-finding study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: This range-finding study included 5 exposure groups and a control. The number and spacing was appropriate.
	Metric 12:	Exposure Route and Method	High	All Outcomes: Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although, in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.
Domain 4: Test Animals	5			
		Contin	nued on nex	ct page

Study Citation: Health	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Renal/Kidney; Endocrine (Endocrine); Reproductive/Developmental; Hepatic/Liver;					
Outcome(s): Reported Health Effect(s):  Duration: Chemical: HERO ID:	Renal/Kidney; Endocrine (Endocrine); Reproductive/Developmental; Hepatic/Liver;  Renal/Kidney: Organ weight, histopathology (urinary bladder, kidney); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology (adrenals, pituitary, pancreas); Reproductive/Developmental: Organ weights (uterus, ovary, testes), histopathology (uterus, ovary, testes, prostate); Hepatic/Liver: organ weights; clinical chemistry (serum SGPT and ALP activity: 90-day study), BSP retention (both durations); in the liver (SGPT activity [preliminary study only], GL-6-Pase, AH and APDM activity [90-day only] and triglyceride content [both durations]); histopathology.; Short-term (>1-30 days) Short-term; 2-weeks 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1772372					
Domain		Metric	Rating	Comments		
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: SPF Wistar rats were used. The animal starting body weights, source, and sex were reported. Age was not specified. The test species were appropriate for the outcomes of interest.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry details were limited to food and water availability and the number of animals per cage (2/cage). Other details (e.g., temperature, humidity, light cycle), were not reported. Insufficient information was provided to determine whether there was consistency across groups.		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The study used 6 male rats/group. The authors did not justify the use of males only. The number of animals/group was sufficient to allow for statistical analysis.		
Domain 5: Outcome A	ssessment					
Domain 3. Outcome A	Metric 16:	Outcome Assessment Methodology	Medium	Renal/Kidney: The outcome assessment methodology available in the report was limited. No methods for histopathology were provided (e.g., tissue fixation methods etc). The methods used were considered to be sensitive for the outcome of interest, although kidney-related clinical chemistry or urinalysis endpoints were not assessed.; Endocrine (Endocrine): The outcome assessment methodology available in the report was limited. No methods for histopathology were provided (e.g., tissue fixation methods etc). The methods used were considered to be sensitive for the outcome of interest.; Reproductive/Developmental: The outcome assessment methodology available in the report was limited. No methods for histopathology were provided (e.g., tissue fixation methods etc). The methods used were considered to be sensitive for the outcome of interest.; Hepatic/Liver: The outcome assessment methodology available in the report was limited. Several other studies were referred to for methods of measuring serum enzymes, liver enzyme activities, and for the BSP retention test. These references were not reviewed for this evaluation as many of these are established, uncomplicated methods. No methods for histopathology were provided (e.g., tissue fixation methods etc). All of the methods were considered to be sensitive for the outcome of interest.		
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Insufficient methodological details were provided to assess consistency.		
	Metric 18:	Sampling Adequacy	High	All Outcomes: All of the surviving animals were sampled for the outcomes of interest.		
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary or required for outcomes that are either not subjective in nature, or are simple measures. Blinding is not recommended for initial histopathological examinations.		
		Contin	nued on nex	rt page		

		···contin	ucu mom p	revious page		
Study Citation: Health Outcome(s):	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Renal/Kidney; Endocrine (Endocrine); Reproductive/Developmental; Hepatic/Liver;  Renal/Kidney: Organ weight, histopathology (urinary bladder, kidney); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology (adrenals, pituitary, pancreas); Reproductive/Developmental: Organ weights (uterus, ovary, testes), histopathology (uterus, ovary, testes, prostate); Hepatic/Liver: organ weights; clinical chemistry (serum SGPT and ALP activity: 90-day study), BSP retention (both durations); in the liver (SGPT activity					
Reported Health Effect(s):						
Duration: Chemical: HERO ID:	Short-term (	>1-30 days) Short-term; 2-weeks bethane- Isomer: 1,2-Dichloroethane	ctivity [90-d	ay only] and triglyceride content [both durations]); histopathology.;		
Domain		Metric	Rating	Comments		
	Metric 20:	Negative Control Response	Medium	Renal/Kidney: The negative control responses were quantitatively reported for some endpoints and were appropriate.; Endocrine (Endocrine): The negative control responses were quantitatively reported for some endpoints and were appropriate.; Reproductive/Developmental: The negative control responses were quantitatively reported for some endpoints and were appropriate.; Hepatic/Liver: The negative control responses were quantitatively reported for some endpoints and were appropriate		
Domain 6: Confoundi	ng / Variable Co	ntrol				
Domain o. Comoundi	Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: The study recorded most information to determine confounding (e.g., body weights and food intake), and there were no differences across groups.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.		
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods in general were described and were appropriate for the datasets.		
	Metric 24:	Reporting of Data	High	Renal/Kidney: Organ weights and other renal/kidney endpoints were reported as means with unspecified measures of variance. Negative histopathology results were qualitatively described in the text.; Endocrine (Endocrine): Organ weights and other Endocrine endpoints were reported as means with unspecified measures of variance. Negative histopathology results were qualitatively described in the text.; Reproductive/Developmental: Organ weights and other Reproductive/Developmental endpoints were reported as means with unspecified measures of variance. Negative histopathology results were qualitatively described in the text.; Hepatic/Liver: Organ weights and other liver endpoints were reported as means with unspecified measures of variance. Negative histopathology results were qualitatively described in the text.		
Overall Qual	ity Detern	nination	High			

<b>Study Citation:</b>	Igwe, O.J., Hee, S.S., Wagner, W.D. (1986). Interaction between 1,2-dichloroethane and disulfiram. I. Toxicologic effects. Fundamental and Applied
	Toxicology 6(4):733-746.
Health	Immune/Hematological; Renal/Kidney; Reproductive/Developmental; Nutritional/Metabolic; Lung/Respiratory; Hepatic/Liver; Mortality;
Outcome(s):	
Reported Health	Immune/Hematological: Relative spleen weight, spleen necropsy and histopathology; Renal/Kidney: Kidney weights were recorded and kidneys
Effect(s):	were examined at histology.; Reproductive/Developmental: Relative testicular weight; testes necropsy/histopathology with incidence of lesions; Nutri-
	tional/Metabolic: Initial and final body weights; body weight change (and associated food consumption) during the 30-d exposure period; Lung/Respiratory:
	Lung weights (this was only reported for the i.p. exposure study); Hepatic/Liver: Relative liver weight; liver necropsy/histopathology with incidence of
	lesions; Mortality: Survival during the 30-day exposure period;
<b>Duration:</b>	Short-term (>1-30 days) 30 days (inhalation)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200386

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature as 1,2 dichloroethane, 1,2-DCE, ethylene dichloride.
	Metric 2:	Test Substance Source	High	All Outcomes: Source: Fisher Scientific Co., Fairlawn, NJ.
	Metric 3:	Test Substance Purity	High	All Outcomes: The percentage purity from each lot determined on a Perkin-Elmer Sigma I gas chromatograph equipped with flame ionization detector was not less than 99.97%.
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Study included concurrent control group animals exposed to vehicle only.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not needed for this type of study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure C	Characterization			
1	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The method and equipment used to generate the test substance as a vapor were reported and appropriate.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and exposures were administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Analytical concentrations did not deviate widely. Effects were observed at the two highest concentrations. The analytical method (ir GA and charcoal analyses) used to measure chamber test substance and vehicle concentration was reported.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose/concentration spacing were explicitly justified with results of the intraperitoneal study.
	Metric 12:	Exposure Route and Method	High	All Outcomes: Whole body inhalation chambers with 48 air changes per hour were used.

Domain 4: Test Animals

<b>Study Citation:</b>	Igwe, O.J., Hee, S.S., Wagner, W.D. (1986). Interaction between 1,2-dichloroethane and disulfiram. I. Toxicologic effects. Fundamental and Applied				
		6(4):733-746.			
Health	Immune/Her	natological; Renal/Kidney; Reproductive/D	evelopment	al; Nutritional/Metabolic; Lung/Respiratory; Hepatic/Liver; Mortality;	
Outcome(s):					
Reported Health	Immune/Hematological: Relative spleen weight, spleen necropsy and histopathology; Renal/Kidney: Kidney weights were recorded and kidneys				
Effect(s):				we testicular weight; testes necropsy/histopathology with incidence of lesions; Nutri-	
				(and associated food consumption) during the 30-d exposure period; Lung/Respiratory:	
				Hepatic/Liver: Relative liver weight; liver necropsy/histopathology with incidence of	
		tality: Survival during the 30-day exposure	period;		
Duration:		>1-30 days) 30 days (inhalation)			
Chemical:		ethane- Isomer: 1,2-Dichloroethane			
HERO ID:	200386				
Domain		Metric	Rating	Comments	
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age at the start of exposure was not reported.	
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were reported and were adequate.	
	3.5 . 1.5	Husbandry Conditions	3.6.11	10.0	
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: There were 10-12 animals per exposure group.	
Domain 5: Outcome As	sessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment was appropriate for the outcomes of interest.	
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcomes were assessed consistently across study groups.	
	Metric 18:	Sampling Adequacy	High	All Outcomes: The study used adequate sampling.	
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this type of study.	
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control groups were adequate.	
Di (- Cfi	- / W: -1-1- C	-41			
Domain 6: Confounding	g / variable Coi Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes Descriptors note was not mass and	
	Metric 21:	and Procedures	Medium	All Outcomes: Respiratory rate was not measured.	
	Metric 22:	Health Outcomes Unrelated to	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that	
		Exposure		there were differences among groups in animal attrition or health outcomes unrelated to	
		<b>F</b>		exposure that could have influenced the outcome assessment.	
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were appropriate for the study outcomes.	
	Metric 24:	Reporting of Data	Low	All Outcomes: Data were not reported for absolute spleen weights	
Overall Qualit	ty Dotorn	ningtion	High		
Over all Quali	iy Detern		High		

·	Metric	Rating	Comments			
HERO ID:	200386					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichlor	oethane				
Duration:	Relative liver weight; liver necropsy/histopathology with incidence of lesions; Short-term (>1-30 days) 30 days (intraperitoneal)					
	i.p. exposure study); Reproductive/Developmental: Relative testicular weight; testes necropsy/histopathology with incidence of lesions; Hepatic/Liver:					
Effect(s):	nal/Kidney: Kidney weights were recorded and kidneys were examined at histology.; Lung/Respiratory: Lung weights (this was only reported for the					
Reported Health	Nutritional/Metabolic: Initial and final	body weights; body weight ch	ange (and associated food consumption) during the 30-d exposure period; Re			
Outcome(s):						
Health	Toxicology 6(4):733-746. Nutritional/Metabolic; Renal/Kidney; Lu	ng/Respiratory; Reproductive/I	Developmental; Hepatic/Liver;			
Study Citation:		986). Interaction between 1,2-0	lichloroethane and disulfiram. I. Toxicologic effects. Fundamental and Applied			

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature as 1,2 dichloroethane, 1,2-DCE, ethylene dichloride.
	Metric 2:	Test Substance Source	High	All Outcomes: Source: Fisher Scientific Co., Fairlawn, NJ.
	Metric 3:	Test Substance Purity	High	All Outcomes: The percentage purity from each lot determined on a Perkin-Elmer Sigma I gas chromatograph equipped with flame ionization detector was not less than 99.97%.
Domain 2: Test Design				
, and the second	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Study included concurrent control group animals exposed to vehicle only.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not needed for this type of study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Cha	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage was not reported and lack of details could substantially impact results since the substance is potentially volatile.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration for the groups are insufficiently reported and the missing information may have an impact on the results.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Exposure doses were reported without ambiguity in Table 1.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: This IP study was performed to establish the duration, target organs, and dosing parameters for the inhalation study. The animals were administered DCE by IP for 30 days.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Only one exposure group was tested.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure reported and suited to the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age at the start of exposure was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Husbandry conditions were reported and were adequate.

### Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

<b>Study Citation:</b>	Igwe, O.J., Hee, S.S., Wagner, W.D. (1986). Interaction between 1,2-dichloroethane and disulfiram. I. Toxicologic effects. Fundamental and Applied
	Toxicology 6(4):733-746.
Health	Nutritional/Metabolic; Renal/Kidney; Lung/Respiratory; Reproductive/Developmental; Hepatic/Liver;

Outcome(s):

Nutritional/Metabolic; Renal/Kidney; Lung/Respiratory; Reproductive/Developmental; Hepatic/Liver;

Reported Health **Effect(s):** 

Nutritional/Metabolic: Initial and final body weights; body weight change (and associated food consumption) during the 30-d exposure period; Renal/Kidney: Kidney weights were recorded and kidneys were examined at histology.; Lung/Respiratory: Lung weights (this was only reported for the i.p. exposure study); Reproductive/Developmental: Relative testicular weight; testes necropsy/histopathology with incidence of lesions; Hepatic/Liver: Relative liver weight; liver necropsy/histopathology with incidence of lesions;

**Duration:** Chemical: HERO ID:

Short-term (>1-30 days) 30 days (intraperitoneal) 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Reporting of Data

200386

HERU ID:	200380			
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: There were 9 animals per dose group. This IP study was performed to establish the duration, target organs, and dosing parameters for the inhalation study.
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment was appropriate for the outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Details regarding food consumption assessment (the effect being evaluated in this form) were not provided in detail.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Details regarding sampling of outcomes were not reported and this defi- ciency is likely to have a substantial impact on results.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this type of study.
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological response of the negative control groups were not reported (results are described in text only and state no effect of treated group on food consumption. No other measures for nutritional measures are reported for animals exposed via i.p.)
Domain 6: Confoun	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine if any confounding variables were observed, the reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were appropriate for the study outcomes.

## **Overall Quality Determination**

Metric 24:

## Medium

Low

All Outcomes: Data for exposure-related findings were not shown for each study group,

but results were described in the text.

Study Citation:

Igwe, O.J., Hee, S.S., Wagner, W.D. (1986). Interaction between 1,2-dichloroethane and tetraethylthiuram disulfide (disulfiram). II. Hepatotoxic manifestations with possible mechanism of action. Toxicology and Applied Pharmacology 86(2):286-297.

Hepatic/Liver

Outcome(s):

Reported Health

Relative liver weight, hepatic reduced glutathione, hepatic enzymes (cytochrome P450 content, cytosolic glutathione S-transferase activity), serum enzymes

Effect(s):

Relative liver weight, hepatic reduced glutathione, hepatic enzymes (cytochrome P450 content, cytosolic glutathione S-transferase activity), serum enzymes (sorbitol dehydrogenase (SDH), ALP, and 5'-nucleotidase). Hepatic DNA and protein content were determined to be mechanistic rather than apical

HERO ID: 200387 Table: 1 of 1

endpoints and are not included in the assessment.

**Duration:** Short-term (>1-30 days) 30 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200387

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified with definitive nomenclature ("1,2-dichloroethane").
	Metric 2:	Test Substance Source	Low	The test substance was obtained from a commercial source. A batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	The test substance was reported to be 99.97% pure, as determined by GCMS.
Domain 2: Test Design				
20114111 21 1434 2431g.1	Metric 4:	Negative and Vehicle Controls	High	Fresh air negative controls were sham-exposed in similar inhalation chambers and the airflow was maintained as for the treated groups.
	Metric 5:	Positive Controls	N/A	No positive control is necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were reported to be assigned to cages using a random numbers table.
Domain 3: Exposure Ch				
	Metric 7:	Preparation and Storage of Test Substance	High	Vapor generation was reported in detail and appropriate. Concentrations were verified analytically.
	Metric 8:	Consistency of Exposure Administration	High	Exposure administration was consistent across treatment groups. Treatment groups were exposed for the same frequency and duration and cages were rotated according to a prepared schedule within the inhalation chamber to ensure uniform exposure.
	Metric 9:	Reporting of Doses/Concentrations	High	Analytical and target concentrations were reported without ambiguity. Analytical concentrations were within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed for 7 hr/day and 5 days/week for 30 days, which is slightly different than typical inhalation studies (usually 6 hr/day and 5 days/week for 28 days), but this is unlikely to have a substantial impact on results.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The LOAEC was the highest dose tested, so the concentrations were not adequate to evaluate a dose-response curve. However, this is not expected to have substantially impacted results, as the concentrations tested were adequate to address the intended purpose of the study, which was to inform the mode-of-action of DCE-induced hepatotoxicity.
	Metric 12:	Exposure Route and Method	Medium	The inhalation route was appropriate for the test substance and study type. The exposure was whole-body for the vapor, which may condense; however, the airflow rate was reported as 344 L/min.

### Domain 4: Test Animals

		contin	ued from p	revious page				
Study Citation:		Hee, S.S., Wagner, W.D. (1986). Interaction possible mechanism of action. Toxicology a		2-dichloroethane and tetraethylthiuram disulfide (disulfiram). II. Hepatotoxic manifes- Pharmacology 86(2):286-297.				
Health	Hepatic/Liver							
Outcome(s):								
Reported Health				cytochrome P450 content, cytosolic glutathione S-transferase activity), serum enzymes				
Effect(s):	(sorbitol del	hydrogenase (SDH), ALP, and 5'-nucleotid	lase). Hepa	atic DNA and protein content were determined to be mechanistic rather than apical				
- ·		d are not included in the assessment.						
Duration:		>1-30 days) 30 days						
Chemical: HERO ID:	1,1-Dichloro 200387	bethane- Isomer: 1,2-Dichloroethane						
Domain		Metric	Rating	Comments				
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported and the animals were obtained from a commercial source.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All animal husbandry conditions were reported and appropriate and there were no differences reported between groups.				
	Metric 15:	Number of Animals per Group	Low	Sample size was $n = 6$ rats per treatment group and $n = 12$ rats for the control group. This is considered adequate for the study duration (short-term) and type. However, it was not specifically stated that these numbers of animals were exposed; the sample sizes were only described in the figure legends. Therefore, Metric 15 is rated Low (not reported) and Metric 18 is rated High.				
D : 5.0 :								
Domain 5: Outcome			*** 1					
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology (liver-related enzymes in whole blood, liver weights) was sensitive and appropriate for the outcomes of interest.				
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across treatment groups. A protocol is provided and efforts were made to reduce bias, such as sacrificing animals in a random sequence.				
	Metric 18:	Sampling Adequacy	High	Sample size was $n = 6$ rats per treatment group and $n = 12$ rats for the control group. This is considered adequate for the study duration (short-term) and type. However, it was not specifically stated that these numbers of animals were exposed; the sample sizes were only described in the figure legends. Therefore, Metric 15 is rated Low (not reported) and Metric 18 is rated High.				
	Metric 19:	Blinding of Assessors	N/A	No subjective outcomes were assessed.				
	Metric 20:	Negative Control Response	High	Negative control responses were appropriate.				
D : ( C C :								
Domain 6: Confound	-		M - J:					
	Metric 21:	Confounding Variables in Test Design	Medium	Respiratory rates were not assessed or reported. This is a potentially confounding factor.				
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	High	No health outcomes unrelated to exposure were reported or identified.				
	Metric 23:	Data Presentation and Analysis	High	Statistical analyses were reported and appropriate for the type of data analyzed (one-way ANOVA with Scheffe's post-hoc test).				
	Metric 24:	Reporting of Data	High	All data were reported adequately for each treatment group and outcome of interest.				
Overall Qua	lity Detern	nination	High					

HERO ID: 5557200 Table: 1 of 3

**Study Citation:** Jin, X., Liao, Y., Tan, X., Guo, J., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of the p38 MAPK signaling pathway in overexpression of matrix metalloproteinase-9 during the course of brain edema in 1,2-dichloroethane-intoxicated mice. NeuroToxicology 69:296-306. Health Neurological/Behavioral Outcome(s): Reported Health Brain weight (wet and dry), blood brain barrier permeability. Effect(s): **Duration:** Short-term (>1-30 days) Up to 3 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical: HERO ID: 5557200 Domain Metric Comments Rating Domain 1: Test Substance Metric 1: Test Substance Identity High Test substance was identified as 1,2-dichloroethane. Metric 2: Test Substance Source Low The source of the test substance was not reported. Metric 3: **Test Substance Purity** High The purity of the test substance was reported to be >99%. Domain 2: Test Design Negative and Vehicle Controls High The negative control was appropriate (sham-treated). Metric 4: Metric 5: Positive Controls N/A Not applicable for this study. Metric 6: Medium Randomized Allocation of Animals Study states animals were randomly allocated into study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low Storage of test substance were not adequately reported given the volatility of the test Substance substance. Metric 8: Consistency of Exposure High Test substance was administered consistently across study groups. Administration Reporting of Doses/Concentrations Metric 9: Low Nominal and target concentrations were not reported. Method used to measure concentration in the chamber was not reported. Metric 10: **Exposure Frequency and Duration** Medium Exposure was for 3.5 hours a day, up to 3 days. Number of Exposure Groups and Metric 11: Medium Only one exposure group was studied, a NOAEL was not obtained. Dose/Concentration Spacing Exposure Route and Method Metric 12: Uninformative A static inhalation chamber was used to deliver test substance. Domain 4: Test Animals Metric 13: Test Animal Characteristics Medium Age of the test animals was not reported. Metric 14: Adequacy and Consistency of Animal Medium Light-dark cycle was not reported. **Husbandry Conditions** Number of Animals per Group Medium Metric 15: The number of animals per study group was not reported. Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology High The outcome assessment methodology addressed the intended outcomes of interest. Metric 17: Consistency of Outcome Assessment High Outcomes were assessed consistently across study groups. Metric 18: Low Sampling Adequacy The number of evaluations per concentration were not reported. Metric 19: Blinding of Assessors N/A Blinding was not necessary.

HERO ID: 5557200 Table: 1 of 3

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**Study Citation:** Jin, X., Liao, Y., Tan, X., Guo, J., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of the p38 MAPK signaling pathway in overexpression of matrix

metalloproteinase-9 during the course of brain edema in 1,2-dichloroethane-intoxicated mice. NeuroToxicology 69:296-306.

Health Neurological/Behavioral

**Outcome(s):** 

**Reported Health** 

Brain weight (wet and dry), blood brain barrier permeability.

Effect(s):

Short-term (>1-30 days) Up to 3 days **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 5557200

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confound	ing / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	High	Data were adequately reported.

## **Overall Quality Determination**

HERO ID: 5557200 Table: 2 of 3

**Study Citation:** Jin, X., Liao, Y., Tan, X., Guo, J., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of the p38 MAPK signaling pathway in overexpression of matrix metalloproteinase-9 during the course of brain edema in 1,2-dichloroethane-intoxicated mice. NeuroToxicology 69:296-306. Health Mortality; Clinical signs (Clinical signs); Outcome(s): Reported Health Mortality: Mortality; Clinical signs (Clinical signs): Poisoning symptoms (tremors, forelimb flexure).; Effect(s): **Duration:** Short-term (>1-30 days) Up to 3 days Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 5557200 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: Test substance was identified as 1,2-dichloroethane. Metric 2: Test Substance Source Low All Outcomes: The source of the test substance was not reported. Metric 3: **Test Substance Purity** High All Outcomes: The purity of the test substance was reported to be >99%. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: The negative control was appropriate (sham-treated). N/A Metric 5: Positive Controls All Outcomes: Not applicable for this study. Metric 6: Randomized Allocation of Animals Medium All Outcomes: Study states animals were randomly allocated into study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low All Outcomes: Storage of test substance were not adequately reported given the volatil-Substance ity of the test substance. Metric 8: Consistency of Exposure High All Outcomes: Test substance was administered consistently across study groups. Administration Reporting of Doses/Concentrations Metric 9: Low All Outcomes: Nominal and target concentrations were not reported. Method used to measure concentration in the chamber was not reported. **Exposure Frequency and Duration** Medium Metric 10: All Outcomes: Exposure was for 3.5 hours a day, up to 3 days. Metric 11: Number of Exposure Groups and Medium All Outcomes: Only one exposure group was studied, a NOAEL was not obtained. Dose/Concentration Spacing Metric 12: Exposure Route and Method Uninformative All Outcomes: A static inhalation chamber was used to deliver test substance. Domain 4: Test Animals Metric 13: Test Animal Characteristics Medium All Outcomes: Age of the test animals was not reported. Metric 14: Adequacy and Consistency of Animal Medium All Outcomes: Light-dark cycle was not reported. **Husbandry Conditions** Medium Metric 15: Number of Animals per Group All Outcomes: The number of animals per study group was not reported. Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology High All Outcomes: The outcome assessment methodology addressed the intended outcomes Metric 17: Consistency of Outcome Assessment High All Outcomes: Outcomes were assessed consistently across study groups. Metric 18: Sampling Adequacy Low All Outcomes: The number of evaluations per concentration were not reported. Metric 19: Blinding of Assessors N/A All Outcomes: Blinding was not necessary. Metric 20: Negative Control Response High All Outcomes: The negative control response was appropriate.

HERO ID: 5557200 Table: 2 of 3

1,1-Dichloroethane

### ... continued from previous page

Study Citation: Jin, X., Liao, Y., Tan, X., Guo, J., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of the p38 MAPK signaling pathway in overexpression of matrix

metalloproteinase-9 during the course of brain edema in 1,2-dichloroethane-intoxicated mice. NeuroToxicology 69:296-306.

**Health** Mortality; Clinical signs (Clinical signs);

Outcome(s):

**Reported Health** Mortality: Mortality; Clinical signs (Clinical signs): Poisoning symptoms (tremors, forelimb flexure).;

Effect(s):

**Duration:** Short-term (>1-30 days) Up to 3 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5557200

Domain		Metric	Rating	Comments
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	Low	Mortality: Mortality data were not shown, but described in the text.; Clinical signs (Clinical signs): Incidence data not reported, described in text.

## **Overall Quality Determination**

HERO ID: 5557200 Table: 3 of 3

Study Citation: Jin, X., Liao, Y., Tan, X., Guo, J., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of the p38 MAPK signaling pathway in overexpression of matrix

metalloproteinase-9 during the course of brain edema in 1,2-dichloroethane-intoxicated mice. NeuroToxicology 69:296-306.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Body weight

Effect(s):

**Duration:** Short-term (>1-30 days) Up to 3 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5557200

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported to be >99%.
Domain 2: Test Desig	gn			
·	Metric 4:	Negative and Vehicle Controls	High	The negative control was appropriate (sham-treated).
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	Study states animals were randomly allocated into study groups.
Domain 3: Exposure	Characterization			
<b>,</b>	Metric 7:	Preparation and Storage of Test Substance	Low	Storage of test substance were not adequately reported given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Nominal and target concentrations were not reported. Method used to measure concentration in the chamber was not reported.
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure was for 3.5 hours a day, up to 3 days.
	Metric 11:	Number of Exposure Groups and	Medium	Only one exposure group was studied, a NOAEL was not obtained.
		Dose/Concentration Spacing		• • •
	Metric 12:	Exposure Route and Method	Uninformative	A static inhalation chamber was used to deliver test substance.
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Medium	Age of the test animals was not reported.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Light-dark cycle was not reported.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group was not reported.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Low	The number of evaluations per concentration were not reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary.
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.

HERO ID: 5557200 Table: 3 of 3

### ... continued from previous page

Study Citation: Jin, X., Liao, Y., Tan, X., Guo, J., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of the p38 MAPK signaling pathway in overexpression of matrix

metalloproteinase-9 during the course of brain edema in 1,2-dichloroethane-intoxicated mice. NeuroToxicology 69:296-306.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Body weight

**Effect(s):** 

**Duration:** Short-term (>1-30 days) Up to 3 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5557200

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variabl	e Control		
Metric	21: Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences.
Metric	22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Metric	23: Data Presentation and Analysis	High	Statistical analysis was appropriate.
Metric	24: Reporting of Data	Medium	Body weight of interim sacrifices were not reported.

## **Overall Quality Determination**

HERO ID: 5431556 Table: 1 of 1

**Study Citation:** Jin, X., Liao, Y., Tan, X., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of CYP2E1 in the course of brain edema induced by subacute poisoning with 1,2-dichloroethane in mice. Frontiers in Pharmacology 9(1317):1317. Health Neurological/Behavioral; Nutritional/Metabolic; Mortality; Outcome(s): Neurological/Behavioral: Behavior, forelimb flexure, edema in brain (histologically and by brain water content), mRNA and protein expression of CYP2E1, Reported Health Effect(s): oxidative stress markers and tight junction proteins in the brain; Nutritional/Metabolic: Body weight; Mortality; Mortality; **Duration:** Short-term (>1-30 days) 3 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical: HERO ID: 5431556 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: Test substance was identified as 1,2-dichloroethane. Metric 2: Test Substance Source Low All Outcomes: The source of the test substance and batch/lot number were not provided. Metric 3: **Test Substance Purity** High All Outcomes: Test substance was more than 99% pure. Domain 2: Test Design Metric 4: Negative and Vehicle Controls Low All Outcomes: Details regarding the negative control are limited. Animals were kept in the chamber without exposure to test substance. N/A Metric 5: Positive Controls All Outcomes: Positive control was not required in this study. Metric 6: Randomized Allocation of Animals Medium All Outcomes: Animals were randomly divided into groups. Domain 3: Exposure Characterization Preparation and Storage of Test Metric 7: Low All Outcomes: Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored. Substance Metric 8: Consistency of Exposure High All Outcomes: Exposure was administered consistently across study groups. Administration Metric 9: Reporting of Doses/Concentrations High All Outcomes: Target and measured concentrations (time-weighted average) were reported. Metric 10: **Exposure Frequency and Duration** Medium All Outcomes: Exposure duration was only 3.5 hours/day. Number of Exposure Groups and Medium Metric 11: All Outcomes: Only one concentration was studied; concentration was justified based on Dose/Concentration Spacing effects in previous publications. Exposure Route and Method Metric 12: Uninformative All Outcomes: A static inhalation chamber was used. Domain 4: Test Animals Metric 13: Test Animal Characteristics Medium All Outcomes: Age was not reported. Metric 14: Adequacy and Consistency of Animal High All Outcomes: Husbandry conditions were adequately reported. **Husbandry Conditions** Number of Animals per Group Medium Metric 15: All Outcomes: The number of animals exposed /group were appropriate for the study type (n=6). Domain 5: Outcome Assessment Metric 16: High Outcome Assessment Methodology All Outcomes: Outcome assessment and methodology were appropriate. Metric 17: Consistency of Outcome Assessment Medium All Outcomes: Details of outcome assessment protocol were limited. Continued on next page ...

Jin, X., Liao, Y., Tan, X., Wang, G., Zhao, F., Jin, Y. (2018). Involvement of CYP2E1 in the course of brain edema induced by subacute poisoning with 1,2-dichloroethane in mice. Frontiers in Pharmacology 9(1317):1317.
Neurological/Behavioral; Nutritional/Metabolic; Mortality;
Neurological/Behavioral: Behavior, forelimb flexure, edema in brain (histologically and by brain water content), mRNA and protein expression of CYP2E1,
oxidative stress markers and tight junction proteins in the brain; Nutritional/Metabolic: Body weight; Mortality: Mortality;
Short-term (>1-30 days) 3 days
1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
5431556

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	High	Neurological/Behavioral: The number of animals evaluated/group was appropriate.; Nutritional/Metabolic: The number of samples evaluated/group was appropriate.; Mortality: The number of samples evaluated/group was appropriate.
	Metric 19:	Blinding of Assessors	N/A	Neurological/Behavioral: Blinding was not necessary for this study.; Nutritional/Metabolic: Blinding was not necessary for this endpoint; Mortality: Blinding was not necessary for this endpoint
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.
Domain 6: Confoundin	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	High	All Outcomes: All outcome data were reported adequately.

# **Overall Quality Determination**

HERO ID: 4492694 Table: 1 of 1

Study Citation:

Li, W., Chen, L., Su, Y., Yin, H., Pang, Y., Zhuang, Z. (2015). 1,2-Dichloroethane induced nephrotoxicity through ROS mediated apoptosis in vitro and in vivo. Toxicology Research 4(5):1389-1399.

Renal/Kidney; Nutritional/Metabolic;

Reported Health

Renal/Kidney: Blood creatinine and urea levels, kidney weight, macroscopic and histopathological evaluation of kidneys, number of apoptotic cells in the kidney and levels of oxidative stress parameters (total antioxidant capacity, superoxide dismutase, malondialdehyde and glutathione); Nutri-

tional/Metabolic: Body weight; **Duration:** Short-term (>1-30 days) 5 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4492694

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was Sigma-Aldrich (ST. Louis, MO). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity of test substance was greater than 99.8%
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: Details regarding the negative control are limited and unclear if mice were sham treated.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly divided into groups.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	All Outcomes: Target and measured concentrations were provided. Data regarding the measured concentration is provided in Supplementary Table 1.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure duration/frequency was appropriate (6 hours/day for 5 days).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Minor limitations regarding concentrations studied (full range of responses was not obtained).
	Metric 12:	Exposure Route and Method	Uninformative	All Outcomes: There is no description of the inhalation chamber used. Study only states "Rats were exposed to DCE 6 h per day for 5 days successively in inhalation chambers".
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Animal characteristics were adequately reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Not all husbandry conditions were reported (light-dark cycles, diet and water availability).
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed /group were appropriate for the study type.

Domain 5: Outcome Assessment

		cont	inued from previou	s page			
Study Citation:	Li, W., Cher	ı, L., Su, Y., Yin, H., Pang, Y., Zhuang, Z. (2015	5). 1,2-Dichloroethar	ne induced nephrotoxicity through ROS mediated apoptosis in vitro and in			
		vivo. Toxicology Research 4(5):1389-1399.					
Health	Renal/Kidne	y; Nutritional/Metabolic;					
Outcome(s):							
Reported Health		Renal/Kidney: Blood creatinine and urea levels, kidney weight, macroscopic and histopathological evaluation of kidneys, number of apoptotic cells					
Effect(s):	in the kidne	ey and levels of oxidative stress parameters (t	otal antioxidant cap	pacity, superoxide dismutase, malondialdehyde and glutathione); Nutri-			
		polic: Body weight;					
Duration:	Short-term (	>1-30 days) 5 days					
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	4492694						
Domain		Metric	Rating	Comments			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodologies were appropriate.			
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details of outcome assessment protocol are adequate.			
	Metric 18:	Sampling Adequacy	Low	All Outcomes: The number of animals evaluated/group was not reported.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.			
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.			
Domain 6: Confound	ing / Variable Co	ntrol					
an or comound	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.			
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed and appropriate.			
	Metric 24:	Reporting of Data	Medium	Renal/Kidney: Absolute kidney weight was not reported. Histology and apoptotic cell numbers were not quantified.; Nutritional/Metabolic: Not all data on body weights reported.			

# **Overall Quality Determination**

HERO ID: 4309 Table: 1 of 2

**Study Citation:** Mccarty, L.P., Flannagan, D.C., Randall, S.A., Johnson, K.A. (1992). Acute toxicity in rats of chlorinated hydrocarbons given via the intratracheal route.

Human & Experimental Toxicology 11(3):173-177.

Health Mortality

**Outcome(s):** 

**Reported Health** Lethality

Effect(s):

**Duration:** Short-term (>1-30 days) Short-term

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4309

Domain		Metric	Rating	Comments
Domain 1: Test Substar	ice			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride.
	Metric 2:	Test Substance Source	High	The source of the test substance was identified as Fischer Scientific, Pittsburgh, PA. The batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	The purity was reported as 99.9% or better (based on manufactures analysis).
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Appropriate negative controls were included.
	Metric 5:	Positive Controls	N/A	A positive control was not needed.
	Metric 6:	Randomized Allocation of Animals	Low	The authors do not report how the animals were allocated.
Domain 3: Exposure Cl	naracterization			
r r	Metric 7:	Preparation and Storage of Test	Low	Preparation and storage conditions were not provided.
	Metric 8:	Substance Consistency of Exposure	High	Test substance was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported as a percentage of the Oral LD50. Authors do not explicitly report the concentration used, but enough information is provided to determine the dose.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency was provided without ambiguity (single exposure).
	Metric 11:	Number of Exposure Groups and	High	The number of exposure groups were appropriate for the purpose of this study.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	The route of exposure was intratracheal. This method was appropriate for the test substance.
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	Medium	Age and the starting body weight were not reported. The strain (Sprague-Dawley) and source (Charles River Laboratory) were provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were provided.
	Metric 15:	Number of Animals per Group	Uninformative	Only one animal /dose was studied. The authors state this was done to minimize the use of animals, however it is difficult to know if observed results would be different if more animals were studied.

### Domain 5: Outcome Assessment

Study Citation: Mccarty, L.P., Flannagan, D.C., Randall, S.A., Johnson, K.A. (1992). Acute toxicity in rats of chlorinated hydrocarbons given via the intratracheal route.

Human & Experimental Toxicology 11(3):173-177.

Health

Mortality

**Outcome(s):** 

Reported Health

Lethality

**Effect(s):** 

**Duration:** Short-term (>1-30 days) Short-term

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4309

Domain	Metric	Rating	Comments
Metric 1	6: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome (lethality).
Metric 1	7: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
Metric 1	8: Sampling Adequacy	Uninformative	Only one animal/dose was studied.
Metric 1	9: Blinding of Assessors	N/A	Lethality was evaluated.
Metric 2	0: Negative Control Response	High	The negative control response was adequate for lethality.
Domain 6: Confounding / Variable	Control		
Metric 2	Confounding Variables in Test Design and Procedures	Medium	Authors did assess if cannula was in trachea at necropsy, other potential confounders were not reported.
Metric 2	2: Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.
Metric 2		N/A	Statistical analysis was not possible with a n=1.
Metric 2	4: Reporting of Data	High	All data were reported.

## **Overall Quality Determination**

Human Health Hazard Animal Toxicology Evaluation HERO ID: 4309 Table: 2 of 2

**Study Citation:** Mccarty, L.P., Flannagan, D.C., Randall, S.A., Johnson, K.A. (1992). Acute toxicity in rats of chlorinated hydrocarbons given via the intratracheal route.

Human & Experimental Toxicology 11(3):173-177.

Health

Lung/Respiratory

**Outcome(s):** 

**Reported Health** 

Histopathology of lung tissue

Effect(s):

Short-term (>1-30 days) Short-term **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4309

	Metric	D 4	-
	Wictie	Rating	Comments
;			
Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride.
Metric 2:	Test Substance Source	Low	The source of the test substance was identified as Fischer Scientific, Pittsburgh, PA. The batch/lot number were not provided.
Metric 3:	Test Substance Purity	High	The purity was reported as 99.9% or better (based on manufactures analysis).
Metric 4:	Negative and Vehicle Controls	High	Appropriate negative controls were included.
Metric 5:	Positive Controls	N/A	A positive control was not needed.
Metric 6:	Randomized Allocation of Animals	Low	The authors do not report how the animals were allocated.
racterization			
	Preparation and Storage of Test	Low	Preparation and storage conditions were not provided.
Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups.
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported as a percentage of the Oral LD50. Authors do not explicitly report the concentration used, but enough information is provided to determine the dose.
Metric 10:	Exposure Frequency and Duration	High	Exposure frequency was provided without ambiguity (single exposure).
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups were appropriate for the purpose of this study.
Metric 12:	Exposure Route and Method	High	The route of exposure was intratracheal. This method was appropriate for the test substance.
Metric 13:	Test Animal Characteristics	Medium	Age and the starting body weight were not reported. The strain (Sprague-Dawley) and source (Charles River Laboratory) were provided.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were provided.
Metric 15:	Number of Animals per Group	Uninformative	Only one animal /dose was studied. The authors state this was done to minimize the use of animals, however it is difficult to know if observed results would be different if more animals were studied.
ssment			
	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome (lethality).
	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 1: Metric 2: Metric 3:  Metric 3:  Metric 4: Metric 5: Metric 6:  acterization Metric 7: Metric 8: Metric 9: Metric 10: Metric 11: Metric 12:  Metric 13: Metric 14: Metric 15:	Metric 2: Test Substance Source  Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  acterization Metric 7: Preparation and Storage of Test Substance Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations  Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Metric 15: Number of Animals per Group  ssment Metric 16: Outcome Assessment Methodology Metric 17: Consistency of Outcome Assessment	Metric 2: Test Substance Source  Metric 3: Test Substance Purity  Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls  Metric 5: Positive Controls  Metric 6: Randomized Allocation of Animals  Low  Adminized Allocation of Animals  Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations  Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 13: Test Animal Characteristics  Medium  Metric 14: Adequacy and Consistency of Animal High Husbandry Conditions  Metric 15: Number of Animals per Group  Uninformative

HERO ID: 4309 Table: 2 of 2

### ... continued from previous page

Study Citation: Mccarty, L.P., Flannagan, D.C., Randall, S.A., Johnson, K.A. (1992). Acute toxicity in rats of chlorinated hydrocarbons given via the intratracheal route.

Human & Experimental Toxicology 11(3):173-177.

Health

Lung/Respiratory

Outcome(s):

Reported Health

Histopathology of lung tissue

**Effect(s):** 

**Duration:** Short-term (>1-30 days) Short-term

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4309

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	Uninformative	Only one animal/dose was studied, therefore only one lung/ dose was evaluated for histological changes.
	Metric 19:	Blinding of Assessors	N/A	Initial histopathology was assessed therefore blinding was not required
	Metric 20:	Negative Control Response	Low	The lung pathology of the volume control was scored "moderate" which was the same as the score given to the test substance group.
Domain 6: Confound	C			
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Authors did assess if cannula was in trachea at necropsy, other potential confounders were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not possible with a n=1.
	Metric 24:	Reporting of Data	High	All data were reported.

## **Overall Quality Determination**

HERO ID: 62637 Table: 1 of 1

Domain 4: Test Animals

Study Citation:		Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.				
Health	Nutritional/I	Metabolic; Hepatic/Liver; Renal/Kidney; Ne	urological/I	Behavioral; Immune/Hematological; Lung/Respiratory;		
<b>Outcome(s):</b>						
Reported Health				r: liver weight, gross necropsy; Renal/Kidney: kidney weight, gross necropsy; Neu-		
Effect(s):	response), co	rological/Behavioral: brain weight, gross necropsy; Immune/Hematological: spleen and thymus weight, hematology, humoral immunity (spleen cell al response), cell mediated immunity (delayed type hypersensitivity), spleen cell response to mitogens, function of reticuloendothelial system, gross necropsy				
D4:	0 1	ratory: lung weight, gross necropsy;				
Duration:	Short-term (>1-30 days) 14 day 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
Chemical: HERO ID:	62637	bethane- Isomer: 1,2-Dichioroethane				
Domain		Metric	Rating	Comments		
Domain 1: Test Substa	ance					
	Metric 1:	Test Substance Identity	High	All Outcomes: test substance identified by nomenclature		
	Metric 2:	Test Substance Source	High	All Outcomes: test substance was obtained from commercial source and lot # provided		
	Metric 3:	Test Substance Purity	Low	All Outcomes: Not reported		
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: vehicle control		
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type		
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: animal allocation was not reported		
Domain 3: Exposure C	Characterization					
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: preparation and storage conditions were incompletely reported but unlikely to affect results		
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: exposures were administered consistently across groups		
	Metric 9:	Reporting of Doses/Concentrations	Low	Nutritional/Metabolic: doses were reported as fraction of LD50; Hepatic/Liver: doses were reported as fraction of LD50; Renal/Kidney: The doses were reported as a fraction of the LD50; Neurological/Behavioral: doses were reported as fraction of LD50; Immune/Hematological: doses were reported as fraction of LD50; Lung/Respiratory: doses were reported as fraction of LD50		
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: administration was appropriate for the study		
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: number of groups was 2 treatment and a control and spacing did not encompass effects		
	Metric 12:	Exposure Route and Method	High	Nutritional/Metabolic: route route and method of exposure was suited to the test substance; Hepatic/Liver: route route and method of exposure was suited to the test substance; Renal/Kidney: route route and method of exposure was suited to the test substance; Neurological/Behavioral: route route and method of exposure was suited to the test substance; Immune/Hematological: 'route and method of exposure was suited to the test substance; Lung/Respiratory: route route and method of exposure was suited to the test substance		

		сопип	uea irom p	revious page		
Study Citation:	Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.					
Health	Nutritional/N	Metabolic; Hepatic/Liver; Renal/Kidney; Ne	urological/I	Behavioral; Immune/Hematological; Lung/Respiratory;		
Outcome(s):						
Reported Health				r: liver weight, gross necropsy; Renal/Kidney: kidney weight, gross necropsy; Neu-		
Effect(s):		rological/Behavioral: brain weight, gross necropsy; Immune/Hematological: spleen and thymus weight, hematology, humoral immunity (spleen cell ab				
		response), cell mediated immunity (delayed type hypersensitivity), spleen cell response to mitogens, function of reticuloendothelial system, gross necropsy;				
	Lung/Respiratory: lung weight, gross necropsy;					
Duration:		>1-30 days) 14 day				
Chemical:		bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	62637					
Domain		Metric	Rating	Comments		
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: animal characteristics were reported except starting body weight, animals were obtained from a commercial source and are appropriate		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: animal husbandry conditions were reported and consistent		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: animal number was reported 10-12/group and was appropriate		
Domain 5: Outcome A						
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: assessment methodology was appropriate for the outcome of interest		
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: outcome assessment was consistent across study groups		
	Metric 18:	Sampling Adequacy	High	All Outcomes: sampling was adequate		
	Metric 19:	Blinding of Assessors	N/A	Nutritional/Metabolic: not necessary; Hepatic/Liver: Not necessary; Renal/Kidney: Not necessary; Neurological/Behavioral: Not necessary; Immune/Hematological: Not necessary; Lung/Respiratory: Not necessary		
	Metric 20:	Negative Control Response	High	All Outcomes: negative controls responded appropriately		
Domain 6: Confoundin	ng / Variable Co	ntrol				
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: there were no reported differences among groups		
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups		
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: methods were described and appropriate		
	Metric 24:	Reporting of Data	High	Nutritional/Metabolic: negative data were reported in text; Hepatic/Liver: data were reported for all groups negative data were reported in text; Renal/Kidney: data were reported for all groups negative data were reported in text; Neurological/Behavioral: data were reported for all groups negative data were reported in text; Immune/Hematological: data were reported for all groups negative data were reported in text; Lung/Respiratory: data were reported for all groups negative data were reported in text		
Overall Quali	ity Detern	nination	High			

**Study Citation:** Pang, Y., Qi, G., Jiang, S., Zhou, Y., Li, W. (2018). 1,2-Dichloroethane induced hepatotoxicity and apoptosis by inhibition of ERK 1/2 pathways. Canadian

Journal of Physiology and Pharmacology 96(11):1119-1126.

Hepatic/Liver Health

**Outcome(s):** 

**Reported Health** Relative liver weight, serum ALT, AST, total cholesterol and triglycerides, histopathology and apoptosis (immunohistochemistry)

Effect(s):

**Duration:** Short-term (>1-30 days) 5 days

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4697150

Test Substance Identity Test Substance Source Test Substance Purity  Negative and Vehicle Controls Positive Controls Randomized Allocation of Animals	High Low High Low N/A	Test substance was identified as 1,2-dichloroethane.  The source of the test substance was Sigma-Aldrich (St. Louis, Missouri). The batch/lot number was not provided.  The purity of test substance was reported to be >99.8%.  It is not clear if the negative control group were untreated or sham treated.
Test Substance Source  Test Substance Purity  Negative and Vehicle Controls Positive Controls	Low High Low	The source of the test substance was Sigma-Aldrich (St. Louis, Missouri). The batch/lot number was not provided.  The purity of test substance was reported to be >99.8%.
Test Substance Purity  Negative and Vehicle Controls Positive Controls	High	number was not provided.  The purity of test substance was reported to be >99.8%.
Negative and Vehicle Controls Positive Controls	Low	
Positive Controls		It is not clear if the negative control group were untreated or sham treated.
Positive Controls		It is not clear if the negative control group were untreated or sham treated.
Positive Controls	N/A	
Randomized Allocation of Animals		A positive control was not needed.
	Medium	Animals were randomly divided into groups.
on		
Preparation and Storage of Test Substance	Low	The preparation and storage of test substance were not reported. Given the volatility of the test substance this information is needed.
Consistency of Exposure	Medium	Details of exposure administration were limited in this study and in cited reference.
Administration Reporting of Doses/Concentrations	Medium	Measured concentrations in chamber were not reported.
Exposure Frequency and Duration	High	Exposure frequency was appropriate (6 hours/day).
Number of Exposure Groups and	High	The number of exposure groups were sufficient to obtain a range of responses.
Dose/Concentration Spacing Exposure Route and Method	Uninformative	The type of inhalation chamber used is not reported. Cited reference also does not report the type of chamber.
Test Animal Characteristics	Medium	Starting body weights were not reported.
Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.
Husbandry Conditions	· ·	, , , ,
	Low	The numbers of animals/group exposure were not reported.
Outcome Assessment Methodology	High	Outcome methodology was appropriate for intended outcomes of interest.
	Medium	Details regarding the outcome assessment protocols were limited; however, this is unlikely to impact results.
	Exposure Route and Method  Test Animal Characteristics Adequacy and Consistency of Animal Husbandry Conditions Number of Animals per Group  Outcome Assessment Methodology Consistency of Outcome Assessment	Exposure Route and Method Uninformative  Test Animal Characteristics Medium Adequacy and Consistency of Animal High Husbandry Conditions Number of Animals per Group Low  Outcome Assessment Methodology High

Study Citation: Pang, Y., Qi, G., Jiang, S., Zhou, Y., Li, W. (2018). 1,2-Dichloroethane induced hepatotoxicity and apoptosis by inhibition of ERK 1/2 pathways. Canadian

Journal of Physiology and Pharmacology 96(11):1119-1126.

Health

Hepatic/Liver

Outcome(s): Reported Health

Relative liver weight, serum ALT, AST, total cholesterol and triglycerides, histopathology and apoptosis (immunohistochemistry)

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 5 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4697150

Domain		Metric	Rating	Comments
N	Metric 18:	Sampling Adequacy	Medium	It is unclear how many animals were evaluated in each group. Study states "Data are presented as means $\pm$ standard deviation for at least 3 replicate experiments per data point." Study does not mention how may animals were in each experimental group. From Figure 1A, it appears each group may have consisted of 10 animals, but this is not clear and not known if different outcomes reflected information from different numbers of animals.
N	Metric 19:	Blinding of Assessors	N/A	Blinding was not needed for the outcomes assessed.
N	Metric 20:	Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / N				
N	Metric 21:	Confounding Variables in Test Design	Low	Test substance is a respiratory irritant and therefore respiratory rate should be reported.
N	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.
N	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
N	Metric 24:	Reporting of Data	Medium	Representative photos of histology and apoptosis are shown without any quantitative analysis to severity.

## **Overall Quality Determination**

Human Health Hazard Animal Toxicology Evaluation

Study Citation:	Plaa, G.L., Larson, R.E. (1965), Rela	ative nephrotoxic properties of chlorinated me	ethane, ethane, and ethylene derivatives in mice.	Toxicology and Applied

Pharmacology 7(1):37-44. Renal/Kidney

Health Renal/Kidney

**Outcome(s):** 

Reported Health

Urinary glucose and protein; renal histopathology

Effect(s):

**Duration:**Short-term (>1-30 days) Short-term- 3 days**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 64411

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure Ch	aracterization			
2 0.1. <b>1.</b> 1.2.1.2.1.200.1.2 0.1.	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	Medium	Details of exposure administration are incomplete.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and	Medium	The one dose studied was the highest one that did not cause lethality.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	Route of exposure was i.p. injection.
			8	
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	Low	The source and age of mice were not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Low	The number of animals/group were not reported.
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	Low	Some details regarding the outcome assessment methodology were lacking (e.g how long urine was collected for, histological evaluations)
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Uninformative	Histology was not performed on controls.
		Cor	ntinued on next page .	

Study Citation: Plaa, G.L., Larson, R.E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied

Pharmacology 7(1):37-44.

Health

Renal/Kidney

Outcome(s):

Reported Health

Urinary glucose and protein; renal histopathology

**Effect(s):** 

**Duration:**Short-term (>1-30 days) Short-term- 3 days**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 64411

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.
	Metric 20:	Negative Control Response	Low	Negative control histology was not reported.
Domain 6: Confounding	ng / Variable Co Metric 21:	ntrol Confounding Variables in Test Design	Low	Potential confounding variables were not reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed; independent statistics could be done.
	Metric 24:	Reporting of Data	Low	Combistix analysis data were not presented.

## **Overall Quality Determination**

Study Citation:	Sherwood, R.L., O'Shea, W., Thomas, P.T., Ratajczak, H.V., Aranyi, C., Graham, J.A. (1987). Effects of inhalation of ethylene dichloride on pulmonary
	defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.

Health

Immune/Hematological

Outcome(s): Reported Health

lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge

Effect(s):

**Duration:** Short-term (>1-30 days) 12d-single dose rats **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200590

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name.
	Metric 2:	Test Substance Source	Low	Source was not reported
	Metric 3:	Test Substance Purity	Medium	purity was not reported; "spectro grade" liquid test substance indicates high purity
Domain 2: Test Desigr	1			
_	Metric 4:	Negative and Vehicle Controls	High	The study authors reported using an appropriate concurrent negative control group.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	animal allocation was not reported
Domain 3: Exposure C	Characterization			
•	Metric 7:	Preparation and Storage of Test	Medium	preparation of the test substance was reported and appropriate. storage was not reported
	Metric 8:	Substance Consistency of Exposure Administration	Medium	details of exposure administration were incompletely reported but appeared to be consistent across groups
	Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and both were appropriate for this study type and the outcomes of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Number of groups was adequate. Spacing was justified by previous data but was not sufficient to identify a response
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were appropriate for the test substance.
Domain 4: Test Anima	ıls			
	Metric 13:	Test Animal Characteristics	High	test animal characteristics were all reported and obtained from commercial source
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All husbandry conditions were reported (including temperature, humidity, light-dark cycle, diet) and were adequate and the same for control and exposed groups.
	Metric 15:	Number of Animals per Group	Low	The number of animals per study group (groups of 10 females) was reported, appropriate for the study type and outcome analysis, and consistent with studies of the same or similar type.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest and the assessment methodology was sensitive and appropriate for the outcomes of interest.

HERO ID: 200590 Table: 1 of 2

### continued from previous page

		***************************************	area moni p	revious page		
Study Citation:	Sherwood, R.L., O'Shea, W., Thomas, P.T., Ratajczak, H.V., Aranyi, C., Graham, J.A. (1987). Effects of inhalation of ethylene dichloride on pulmonary defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.					
Health	Immune/Hematological					
Outcome(s):						
Reported Health	lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge					
Effect(s):	7 1 7 7					
<b>Duration:</b>	Short-term (>1-30 days) 12d-single dose rats					
Chemical:	1,1-Dichloro	pethane- Isomer: 1,2-Dichloroethane				
HERO ID:	200590					
Domain		Metric	Rating	Comments		
	Metric 17:	Consistency of Outcome Assessment	Medium	outcome assessment were previously cited and briefly described and appeared to be carried out consistently across groups		
	Metric 18:	Sampling Adequacy	Low	The information supplied indicates the use of adequate sampling for the outcomes of interest.		
	Metric 19:	Blinding of Assessors	N/A	Not necessary		
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate.		
Domain 6: Confoundir	ng / Variable Co	ntrol				
20 0. 000	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	information reported was not complete, but did not indicate any differences		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss any differences		
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described and sufficient data (e.g., means with standard deviations) were provided to conduct an independent statistical analysis.		
	Metric 24:	Reporting of Data	Medium	negative data was described in text		

Reported Health Effect(s):  Duration: Chemical: I,1-Dichloroethane- Isomer: 1,2-Dichloroethane HERO ID:  Domain 1: Test Substance Metric 2: Test Substance Surve Metric 3: Test Substance Purity Medium  Domain 2: Test Design Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals Low Preparation of the test substance was reported and appropriate. storage was not reported Substance was not reported Not necessary for the study type animal allocation was not reported and appropriate. storage was not reported Netric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Medium Preparation of the test substance was reported and appropriate. storage was not reported Substance  Nedium Preparation of the test substance was reported and appropriate. storage was not reported Substance  Nedium Preparation of the test substance was reported and appropriate. storage was not reported Substance	Study Citation: Health	defenses of mice and rats. Toxicology and Applied Pharmacology 91(3):491-496.  Immune/Hematological  utcome(s):  eported Health lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge  ffect(s):						
Effect(s): Duration: Short-term (>1-30 days) 5d-single dose mouse Chemical: 1,1-Dichlorve-thane- Isomer: 1,2-Dichloroethane HERO ID: 200590  Domain	* *							
Duration:       Short-term (>1-30 days) 5d-single dose mouse         Chemical:       1,1-Dichloroethane- Isomer: 1,2-Dichloroethane         HERO ID:       200590         Domain       Metric       Rating       Comments         Domain 1: Test Substance       Metric 1:       Test Substance Identity       High       The test substance was identified definitively by name.         Metric 2:       Test Substance Source       Low       Source was not reported         Metric 3:       Test Substance Purity       Medium       purity was not reported; "spectro grade" liquid test substance indicates high purity         Domain 2: Test Design       Metric 4:       Negative and Vehicle Controls       High       The study authors reported using an appropriate concurrent negative control group.         Metric 5:       Positive Controls       N/A       Not necessary for the study type         Domain 3: Exposure Characterization       Metric 6:       Randomized Allocation of Animals       Low       animal allocation was not reported         Domain 3: Exposure Characterization       Metric 8:       Preparation and Storage of Test       Medium       preparation of the test substance was reported and appropriate. storage was not reported         Metric 8:       Consistency of Exposure       Medium across groups       Medium across groups       Medium across groups       Medium acr	_							
Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane HERO ID: 200590    Domain	` '							
Domain 1: Test Substance  Metric 1: Test Substance Identity High The test substance was identified definitively by name.  Metric 2: Test Substance Source Low Source was not reported Metric 3: Test Substance Purity Medium purity was not reported; "spectro grade" liquid test substance indicates high purity  Domain 2: Test Design  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals Low animal allocation was not reported  Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations  Metric 9: Reporting of Doses/Concentrations High The exposure frequency and duration of exposure were reported and both were appropriate for the exposure frequency and duration of exposure were reported and both were appropriate. High The exposure frequency and duration of exposure were reported and both were appropriate.	Chemical:	5 · · · · · · · · · · · · · · · · · · ·						
Domain 1: Test Substance  Metric 1: Test Substance Identity High Source was identified definitively by name.  Metric 2: Test Substance Source Low Source was not reported Metric 3: Test Substance Purity Medium purity was not reported; "spectro grade" liquid test substance indicates high purity  Domain 2: Test Design  Metric 4: Negative and Vehicle Controls High The study authors reported using an appropriate concurrent negative control group.  Metric 5: Positive Controls N/A Not necessary for the study type Metric 6: Randomized Allocation of Animals Low animal allocation was not reported  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Medium preparation of the test substance was reported and appropriate. storage was not reported  Metric 8: Substance Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations  Metric 9: Reporting of Doses/Concentrations  Metric 10: Exposure Frequency and Duration High The exposure frequency and duration of exposure were reported and both were appropriate.	HERO ID:	200590						
Metric 1: Test Substance Identity Metric 2: Test Substance Source Metric 3: Test Substance Source Metric 3: Test Substance Purity Medium purity was not reported Medium purity was not reported; "spectro grade" liquid test substance indicates high purity  Domain 2: Test Design  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Medium preparation of the test substance was reported and appropriate. storage was not reported  Medium preparation of the test substance was reported and appropriate. storage was not reported  Medium details of exposure administration were incompletely reported but appeared to be constant tent across groups  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 4: Negative and Vehicle Controls High The study authors reported using an appropriate concurrent negative control group.  Not necessary for the study type animal allocation was not reported  Medium preparation of the test substance was reported and appropriate. storage was not reported  Medium details of exposure administration were incompletely reported but appeared to be constant across groups  Metric 9: Reporting of Doses/Concentrations High The exposure frequency and duration of exposure were reported and both were appropriate.	Domain		Metric	Rating	Comments			
Metric 2: Test Substance Source Metric 3: Test Substance Purity Medium purity was not reported Medium purity was not reported; "spectro grade" liquid test substance indicates high purity  Domain 2: Test Design  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 4: Negative and Vehicle Controls High The study authors reported using an appropriate concurrent negative control group. N/A Not necessary for the study type animal allocation was not reported  Medium preparation of the test substance was reported and appropriate. storage was not reported  Medium details of exposure administration were incompletely reported but appeared to be consument across groups  Medium details of exposure administration were incompletely reported but appeared to be consument across groups  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 9: Reporting of Doses/Concentrations High The exposure frequency and duration of exposure were reported and both were appropriate.	Domain 1: Test Substan	ce						
Domain 2: Test Design  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure  Metric 8: Reporting of Doses/Concentrations Metric 9: Reporting of Doses/Concentrations Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 10: Exposure Frequency and Duration  Medium purity was not reported; "spectro grade" liquid test substance indicates high purity  Medium purity was not reported; "spectro grade" liquid test substance indicates high purity  Medium appropriate concurrent negative control group.  N/A Not necessary for the study type  Low animal allocation was not reported  Medium preparation of the test substance was reported and appropriate. storage was not reported  Medium details of exposure administration were incompletely reported but appeared to be constant across groups  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 10: Test Design  High Administered doses were reported without ambiguity.  The exposure frequency and duration of exposure were reported and both were appropriate.  The study authors reported using an appropriate concurrent negative control group.  N/A Not necessary for the study type  Low animal allocation was not reported  Medium preparation of the test substance was reported and appropriate. storage was not reported  Medium details of exposure administration were incompletely reported but appeared to be constant.		Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name.			
Domain 2: Test Design  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure  Metric 8: Reporting of Doses/Concentrations  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 7: Preparation and Storage of Test Medium Me		Metric 2:	Test Substance Source	Low	Source was not reported			
Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance Consistency of Exposure  Medium Metric 8: Consistency of Exposure  Medium Metric 9: Reporting of Doses/Concentrations Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 4: Negative and Vehicle Controls N/A Not necessary for the study type  animal allocation was not reported  N/A Not necessary for the study type  Animal allocation was not reported  Medium  Medium  Medium  Metric 9: Medium  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 10: The study authors reported using an appropriate concurrent negative control group.  N/A Not necessary for the study type  Animal allocation was not reported  Medium  Medium  Medium  Metric 8: Medium  Metric 9: Reporting of Doses/Concentrations  High  Administered doses were reported without ambiguity.  High  The exposure frequency and duration of exposure were reported and both were appropriate.		Metric 3:	Test Substance Purity	Medium	purity was not reported; "spectro grade" liquid test substance indicates high purity			
Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance Consistency of Exposure  Medium Metric 8: Consistency of Exposure  Medium Metric 9: Reporting of Doses/Concentrations Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 4: Negative and Vehicle Controls N/A Not necessary for the study type  animal allocation was not reported  N/A Not necessary for the study type  Animal allocation was not reported  Medium  Medium  Medium  Metric 8: Medium  Metric 9: Reporting of Doses/Concentrations Medium  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 10: The study authors reported using an appropriate concurrent negative control group.  N/A Not necessary for the study type  Animal allocation was not reported  Medium  Medium  Medium  Medium  Metric 8: Medium  Metric 9: Reporting of Doses/Concentrations  High  Administered doses were reported without ambiguity.  High  The exposure frequency and duration of exposure were reported and both were appropriate.	Domain 2: Test Design							
Metric 5: Positive Controls M/A Not necessary for the study type Metric 6: Randomized Allocation of Animals Low animal allocation was not reported  Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 5: N/A Not necessary for the study type  Animal allocation was not reported  Medium preparation of the test substance was reported and appropriate. storage was not reported  Medium details of exposure administration were incompletely reported but appeared to be consistency of Exposure administration were reported without ambiguity.  High The exposure frequency and duration of exposure were reported and both were appropriate. Storage was not reported and both were appropriate. Storage was not reported but appeared to be consistency of Exposure administration were incompletely reported but appeared to be consistency of Exposure administration were reported without ambiguity.  High The exposure frequency and duration of exposure were reported and both were appropriate.		Metric 4:	Negative and Vehicle Controls	High	The study authors reported using an appropriate concurrent negative control group.			
Domain 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Medium preparation of the test substance was reported and appropriate. storage was not reported to the test substance was reported and appropriate appeared to be consistency of Exposure Medium details of exposure administration were incompletely reported but appeared to be consistency of Exposure were reported without ambiguity.  High The exposure frequency and duration of exposure were reported and both were appropriate.		Metric 5:	Positive Controls		Not necessary for the study type			
Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Medium Med		Metric 6:	Randomized Allocation of Animals	Low	animal allocation was not reported			
Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Medium Med	Domain 3: Evnosure Ch	paracterization						
Substance Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Substance Medium details of exposure administration were incompletely reported but appeared to be constent across groups tent across groups High Administered doses were reported without ambiguity. High The exposure frequency and duration of exposure were reported and both were appropriately and provided in the constant across groups.  Metric 10: Exposure Frequency and Duration  High The exposure frequency and duration of exposure were reported and both were appropriately across groups.	Domain 3. Exposure Cir		Preparation and Storage of Test	Medium	preparation of the test substance was reported and appropriate, storage was not reported			
Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration Medium details of exposure administration were incompletely reported but appeared to be constent across groups High Administered doses were reported without ambiguity. High The exposure frequency and duration of exposure were reported and both were appropriately and provided in the constant across groups  High The exposure frequency and duration of exposure were reported and both were appropriately reported but appeared to be constant.		Wiedle 7.	1	Modrain	preparation of the test substance was reported and appropriate, storage was not reported			
Metric 9: Reporting of Doses/Concentrations High Administered doses were reported without ambiguity.  Metric 10: Exposure Frequency and Duration High The exposure frequency and duration of exposure were reported and both were appropriately appropriate to the content of the co		Metric 8:	Consistency of Exposure	Medium	details of exposure administration were incompletely reported but appeared to be consis-			
Metric 10: Exposure Frequency and Duration High The exposure frequency and duration of exposure were reported and both were appropriate the exposure frequency and duration of exposure were reported and both were appropriate to the exposure frequency and duration of exposure were reported and both were appropriate to the exposure frequency and duration of exposure frequency and duration of exposure frequency and duration of exposure were reported and both were appropriate to the exposure frequency and duration of exposure frequency and					• •			
				_				
		Metric 10:	Exposure Frequency and Duration	High				
Metric 11: Number of Exposure Groups and Low Number of groups was single dose and control. Spacing was justified by previous data but was not sufficient to identify a response		Metric 11:		Low	Number of groups was single dose and control. Spacing was justified by previous data but was not sufficient to identify a response			
Metric 12: Exposure Route and Method High The route and method of exposure were reported and were appropriate for the test sub		Metric 12:		High	The route and method of exposure were reported and were appropriate for the test sub-			
stance.					stance.			
Domain 4: Test Animals	Domain 4: Test Animals							
Metric 13: Test Animal Characteristics High test animal characteristics were all reported and obtained from commercial source				_				
Metric 14: Adequacy and Consistency of Animal Medium All husbandry conditions were reported (including temperature, humidity, light- dark cycle, diet) and were adequate and the same for control and exposed groups.		Metric 14:		Medium				
		Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (groups of 10 females) was reported, appropriate for the study type and outcome analysis, and consistent with studies of the same or similar type.			
Domain 5: Outcome Assessment	Domain 5: Outcome As	ceccment						
Metric 16: Outcome Assessment Methodology High The outcome assessment methodology addressed the intended outcomes of interest an	Domain 3. Outcome Ass		Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest and the assessment methodology was sensitive and appropriate for the outcomes of interest.			
Metric 17: Consistency of Outcome Assessment Medium outcome assessment were previously cited and briefly described and appeared to be carried out consistently across groups		Metric 17:	Consistency of Outcome Assessment	Medium	outcome assessment were previously cited and briefly described and appeared to be			
Continued on next page			Conti	nued on nex	at page			

Study Citation:		_	-	i, C., Graham, J.A. (1987). Effects of inhalation of ethylene dichloride on pulmonar		
TT 1/1.		mice and rats. Toxicology and Applied Phar	macology 9	1(3):491-496.		
Health	Immune/Hei	matological				
Outcome(s):						
Reported Health	lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge					
Effect(s):						
<b>Duration:</b>	Short-term (>1-30 days) 5d-single dose mouse					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	200590					
Domain		Metric	Rating	Comments		
	Metric 18:	Sampling Adequacy	High	The information supplied indicates the use of adequate sampling for the outcomes of interest.		
	Metric 19:	Blinding of Assessors	N/A	Not necessary		
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate.		
Domain 6: Confoundi	-					
	Metric 21:	Confounding Variables in Test Design	Medium	information reported was not complete, but did not indicate any differences		
	Metric 22:	and Procedures Health Outcomes Unrelated to	Medium	There was no information either to support or dismiss any differences		
	Metric 23:	Exposure Data Presentation and Analysis	High	Statistical methods were described and sufficient data (e.g., means with standard deviations) were provided to conduct an independent statistical analysis.		
	Metric 24:	Reporting of Data	High	data were reported for all groups and outcomes, and negative data was described in text		

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Mortality; Hepatic/Liver; Renal/Kidney; Nutritional/Metabolic;

**Outcome(s): Reported Health** 

Mortality: Death; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Renal/Kidney: Gross

HERO ID: 62617 Table: 1 of 3

Effect(s): examinations; histology; organ weights; Nutritional/Metabolic: Body weight; food consumption;

**Duration: Chemical:** 

Short-term (>1-30 days) Short-term 1-10 days; Guinea pigs 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 

62617

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity ≥99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig	ŗn			
	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: Although the methods indicate both unexposed and air-only controls were used, limited details on THIS experiment suggest only unexposed controls may have been used. This is generally not an appropriate control for an inhalation study.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to groups, howeve all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure	Characterization			
Domain 3. Exposure	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results, particularly for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Uninformative	All Outcomes: Conditions between exposed animals and controls were not consistent. 1,700-liters box was used for exposure. Unexposed controls were maintained in standar animal quarters.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Animals were exposed 7hrs/day for 1, 3,4, and 10 days. The short-term duration was done because longer durations resulted in 100% mortality.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Justification of the exposure levels was not provided. This concentration was fatal at longer durations of exposure.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported.

#### Continued on next page ...

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Mortality; Hepatic/Liver; Renal/Kidney; Nutritional/Metabolic;

Outcome(s):

Reported Health Me

Mortality: Death; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Renal/Kidney: Gross

**Effect(s):** examinations; histology; organ weights; Nutritional/Metabolic: Body weight; food consumption;

**Duration:** Short-term (>1-30 days) Short-term 1-10 days; Guinea pigs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

HERO ID:	62617			
Domain		Metric	Rating	Comments
Domain 4: Test Anima	ıls			
	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Animals were reported to come from commercial sources; however, No details on animal strain, age, or starting body weights were provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to reporting the diets provided. No other data were provided.
	Metric 15:	Number of Animals per Group	Low	All Outcomes: Only 2 males were used at each exposure level
Domain 5: Outcome A	ssessment			
Domain 3. Gutcome 1.	Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: It is unclear whether animals were killed immediately following the last exposure, or if a post-exposure observation period was included in the study design. This could have a substantial impact on study results.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: It is not clearly reported whether exposed and untreated controls were consistently assessed.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Specific details regarding sampling of outcomes not clearly reported
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Low	All Outcomes: Details of the biological responses of controls were not provided.
D : ( C f 1:	/W : 11 C	. 1		
Domain 6: Confounding	-		3.6.12	
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information on health outcomes unrelated to exposure was reported.
	Metric 23:	Data Presentation and Analysis	Low	All Outcomes: The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant. Data were qualitatively reported precluding the ability to perform independent statistical analysis.
	Metric 24:	Reporting of Data	Uninformative	Mortality: Mortality results were not reported. The text indicates that animals were killed after 1,3,4, and 10 exposures. It is unknown if any animals died on their own.; Hepatic/Liver: Liver changes (increased liver weights and histopathological changes were reported but did not distinguish which short-term duration exposure group (1, 3, 4, or 10 days) exhibited these results, or how many males were affected.; Renal/Kidney: kidney weight and histopathology changes were reported but did not distinguish which short-term duration exposure group (1, 3, 4, or 10 days) exhibited these results, or how many males were affected.; Nutritional/Metabolic: Body weight changes were reported but did not distinguish which short-term duration exposure group (1, 3, 4, or 10 days) exhibited these results, or how many males were affected. The significance was not indicated.

#### Continued on next page ...

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

HERO ID: 62617 Table: 1 of 3

#### ... continued from previous page

Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on **Study Citation:** 

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Mortality; Hepatic/Liver; Renal/Kidney; Nutritional/Metabolic;

**Outcome(s):** 

Reported Health Mortality: Death; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Renal/Kidney: Gross

Effect(s): examinations; histology; organ weights; Nutritional/Metabolic: Body weight; food consumption;

**Duration:** Short-term (>1-30 days) Short-term 1-10 days; Guinea pigs

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain Metric Rating Comments

## **Overall Quality Determination**

HERO ID: 62617 Table: 2 of 3

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493. Health Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic; Outcome(s): Reported Health Renal/Kidney: Gross examinations; histology; organ weights; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and Effect(s): esterified cholesterol; Nutritional/Metabolic: Body weight; food consumption; **Duration:** Short-term (>1-30 days) Short-term 1-10 days; rats Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 62617 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: High Test Substance Identity All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided Metric 2: Test Substance Source High All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra. Metric 3: **Test Substance Purity** High All Outcomes: Purity ≥99.7 %; the only impurity identified was trichloroethylene. Domain 2: Test Design Metric 4: Negative and Vehicle Controls Low All Outcomes: Although the methods indicate both unexposed and air-only controls were used, limited details on THIS experiment suggest only unexposed controls may have been used. This is generally not an appropriate control for an inhalation study. Positive Controls N/A Metric 5: All Outcomes: Not necessary for the study type Metric 6: Randomized Allocation of Animals Low All Outcomes: The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be wellmatched with experimental animals in respect to number, age, sex, and body weight. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test Substance substance is a volatile chemical, and this could substantially impact results, particularly for a long-term study. Metric 8: Consistency of Exposure Uninformative All Outcomes: Conditions between exposed animals and controls were not consistent. A 1,700-liters box was used for exposure. Unexposed controls were maintained in standard Administration animal quarters. Metric 9: Reporting of Doses/Concentrations High All Outcomes: All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration. Medium Metric 10: **Exposure Frequency and Duration** All Outcomes: Animals were exposed 7hrs/day for 2 or 3 days. The short-term duration was done since longer durations resulted in 100% mortality. Metric 11: Number of Exposure Groups and Medium All Outcomes: Justification of the exposure levels was not provided. This concentration was fatal at longer durations of exposure. Dose/Concentration Spacing Metric 12: Exposure Route and Method Low All Outcomes: Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported. Domain 4: Test Animals Continued on next page ...

			itinuea from previous			
Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.					
Health	Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic;					
Outcome(s):						
Reported Health	Renal/Kidne	y: Gross examinations; histology; organ weig	hts; Hepatic/Liver: Gro	oss examinations; histology; organ weights; liver lipid analysis; free and		
Effect(s):	esterified cho	olesterol; Nutritional/Metabolic: Body weight:	; food consumption;			
Duration:	Short-term (	>1-30 days) Short-term 1-10 days; rats	•			
Chemical:		bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	62617					
Domain		Metric	Rating	Comments		
	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Animals were reported to come from commercial sources; however, No details on animal strain, age, or starting body weights were provided. The text indicates both sexes were used.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to reporting the diets provided. No other data were provided.		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals was appropriate (20/sex)		
Domain 5, Outree A	\ aaaaama=+					
Domain 5: Outcome A	Assessment Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: It is unclear whether enimals were killed immediately fallowing the last		
	Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: It is unclear whether animals were killed immediately following the last exposure, or if a post-exposure observation period was included in the study design. This could have a substantial impact on study results.		
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: It is not clearly reported whether exposed and untreated controls were consistently assessed.		
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Specific details regarding sampling of outcomes not clearly reported		
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the outcomes assessed.		
	Metric 20:	Negative Control Response	Low	All Outcomes: Details of the biological responses of controls were not provided.		
Domain 6: Confoundi	ng / Variable Co	ntrol				
Domain o. Comoundi	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: No confounding variables were reported.		
	Metric 22:	and Procedures Health Outcomes Unrelated to	Medium	All Outcomes: No information on health outcomes unrelated to exposure was reported.		
		Exposure				
	Metric 23:	Data Presentation and Analysis	Low	All Outcomes: The text indicates that T-tests were performed comparing exposed group to air-exposed or unexposed controls where relevant. Data were qualitatively reported		
				precluding the ability to perform independent statistical analysis.		
	Metric 24:	Reporting of Data	Uninformative	Renal/Kidney: A slight increase in kidney weight was reported in the text but did not distinguish whether effects were observed in males or females, or from the 2 or 3-day exposure duration; the significance is not clearly stated. The text indicates no significant differences in blood parameters were observed but does not specify which controls were used for comparison.; Hepatic/Liver: Liver changes (slight increase in weight, histopathological changes) were described in the text but did not distinguish whether		
				effects were observed in males or females, or from the 2 or 3-day duration. The significance of the effects is not clearly stated. The text indicates no significant differences in blood parameters were observed but does not specify which controls were used for corparison.; Nutritional/Metabolic: Rapid loss in BW was reported in the text but did not distinguish whether effects were observed in males or females, or from the 2 or 3-day exposure duration. The significance of the effects is not clearly stated.		

1,1-Dichloroethane

Human Health Hazard Animal Toxicology Evaluation HERO ID: 62617 Table: 2 of 3

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**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic;

**Outcome(s):** 

Reported Health Renal/Kidney: Gross examinations; histology; organ weights; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and

Effect(s): esterified cholesterol; Nutritional/Metabolic: Body weight; food consumption;

**Duration:** Short-term (>1-30 days) Short-term 1-10 days; rats Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain Metric Rating Comments

**Overall Quality Determination** 

HERO ID: 62617 Table: 3 of 3

**Study Citation:** 

Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Mortality

**Outcome(s):** 

Reported Health

Death

Effect(s):

**Duration:** Short-term (>1-30 days) Short-term 1-10 days; rats **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	62617			
Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity ≥99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig	n			
20 11 10 10 10 10 10 10 10 10 10 10 10 10	Metric 4:	Negative and Vehicle Controls	Low	Although the methods indicate both unexposed and air-only controls were used, limited details on THIS experiment suggest only unexposed controls may have been used. This is generally not an appropriate control for an inhalation study.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results, particularly for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Uninformative	Conditions between exposed animals and controls were not consistent. A 1,700-liters box was used for exposure. Unexposed controls were maintained in standard animal quarters.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were exposed 7hrs/day for 2 or 3 days. The short-term duration was done since longer durations resulted in 100% mortality.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Justification of the exposure levels was not provided. This concentration was fatal at longer durations of exposure.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported.
Domain 4: Test Anim	als			
	Metric 13:	Test Animal Characteristics	Low	Animals were reported to come from commercial sources; however, No details on animal strain, age, or starting body weights were provided. The text indicates both sexes were used.
		Cor	ntinued on next page .	•••

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Mortality

**Outcome(s):** 

**Reported Health** 

Death

Effect(s):

Short-term (>1-30 days) Short-term 1-10 days; rats **Duration:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting the diets provided. No other data were provided.
	Metric 15:	Number of Animals per Group	Medium	The number of animals was appropriate (20/sex)
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Low	It is unclear whether animals were killed immediately following the last exposure, or if a post-exposure observation period was included in the study design. This could have a substantial impact on study results.
	Metric 17:	Consistency of Outcome Assessment	Low	It is not clearly reported whether exposed and untreated controls were consistently assessed.
	Metric 18:	Sampling Adequacy	Low	Specific details regarding sampling of outcomes not clearly reported
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Low	Details of the biological responses of controls were not provided.
Domain 6: Confoundin	o / Variable Co	ntrol		
Bomain o. Comounain	Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.
		and Procedures	1/10/01/01	To comounting variables were reported.
	Metric 22:	Health Outcomes Unrelated to	Medium	No information on health outcomes unrelated to exposure was reported.
		Exposure		
	Metric 23:	Data Presentation and Analysis	Uninformative	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant, however, statistical significance for this outcome was not reported, and data enabling an independent statistical analysis was not provided.
	Metric 24:	Reporting of Data	Uninformative	Percent mortality of exposed animals (60%) was reported; however, it the result does not distinguish between males or females, or if it is from the 2 or 3 day exposure durations groups. It is not indicated if any deaths were observed in controls.

### **Overall Quality Determination**

**Study Citation:** Sun, Q., Wang, G., Gao, L., Shi, L., Qi, Y., Lv, X., Jin, Y. (2016). Roles of CYP2e1 in 1,2-dichloroethane-induced liver damage in mice. Environmental

Toxicology 31(11):1430-1438. Nutritional/Metabolic; Mortality; Health

**Outcome(s):** 

**Reported Health** Nutritional/Metabolic: Body weights in Part 1 (3 doses); Mortality: Only in Part 1 (3 doses);

Effect(s):

**Duration:** Short-term (>1-30 days) 10 days- Part 1, 3 concentrations

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was Shanghai Chemical Co. (Shanghai China). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was more than 99% pure.
Domain 2: Test Design				
2011 <b>4</b> 1434 2434g.1	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: Details regarding the negative control are limited and unclear if mice sham treated.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not necessary for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly divided into groups.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Only target concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Exposure duration was only 3.5 hours/day (10 days).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Concentrations were adequate to obtain a range of responses.
	Metric 12:	Exposure Route and Method	Uninformative	All Outcomes: A static inhalation chamber was used.
Domain 4: Test Animals	2			
Domain 1. 10st / minutes	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age was not reported
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Husbandry conditions were adequately reported.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed /group were appropriate for the study type.
Domain 5: Outcome Ass	sessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methodology was appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details of outcome assessment protocol are adequate.
	Metric 18:	Sampling Adequacy	High	All Outcomes: The number of animals evaluated/group was appropriate.

Study Citation: Sun, Q., Wang, G., Gao, L., Shi, L., Qi, Y., Lv, X., Jin, Y. (2016). Roles of CYP2e1 in 1,2-dichloroethane-induced liver damage in mice. Environmental

Toxicology 31(11):1430-1438.

**Health** Nutritional/Metabolic; Mortality;

**Outcome(s):** 

**Reported Health** Nutritional/Metabolic: Body weights in Part 1 (3 doses); Mortality: Only in Part 1 (3 doses);

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 10 days- Part 1, 3 concentrations

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4451633

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
]	Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.
Domain 6: Confounding /	Variable Cor Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.
1	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
]	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed and appropriate.
]	Metric 24:	Reporting of Data	High	All Outcomes: All outcome data were reported adequately.

### **Overall Quality Determination**

HERO ID: 4451633 Table: 2 of 3

**Study Citation:** Sun, Q., Wang, G., Gao, L., Shi, L., Qi, Y., Lv, X., Jin, Y. (2016). Roles of CYP2e1 in 1,2-dichloroethane-induced liver damage in mice. Environmental

Toxicology 31(11):1430-1438. Hepatic/Liver

Health

**Outcome(s):** 

**Reported Health** 

Liver damage after subacute exposure to 1,2- DCE

Effect(s):

Short-term (>1-30 days) 10 days- Part 1, 3 concentrations **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was Shanghai Chemical Co. (Shanghai, China). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	Test substance was more than 99% pure.
Domain 2: Test Desig	'n			
	Metric 4:	Negative and Vehicle Controls	Low	Details regarding the negative control are limited and unclear if mice sham treated.
	Metric 5:	Positive Controls	N/A	Positive control was not necessary for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly divided into groups.
Domain 3: Exposure	Characterization			
Boniam 3. Exposure	Metric 7:	Preparation and Storage of Test Substance	Low	Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored.
	Metric 8:	Consistency of Exposure	High	Exposure was administered consistently across study groups.
	<b>M</b> 0	Administration	T	
	Metric 9:	Reporting of Doses/Concentrations	Low	Only target concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure duration was only 3.5 hours/day (10 days).
	Metric 11:	Number of Exposure Groups and	High	Concentrations were adequate to obtain a range of responses.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	Uninformative	A static inhalation chamber was used.
Domain 4: Test Anim	uale			
Domain 4. Test Aimi	Metric 13:	Test Animal Characteristics	Medium	Age was not reported
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.
		Husbandry Conditions	_	
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed /group were appropriate for the study type.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Histopathology was not performed on liver.
	Metric 17:	Consistency of Outcome Assessment	High	Details of outcome assessment protocol are adequate.
	Metric 18:	Sampling Adequacy	High	The number of animals evaluated/group was appropriate.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.

HERO ID: 4451633 Table: 2 of 3

1,1-Dichloroethane

#### ... continued from previous page

Study Citation: Sun, Q., Wang, G., Gao, L., Shi, L., Qi, Y., Lv, X., Jin, Y. (2016). Roles of CYP2e1 in 1,2-dichloroethane-induced liver damage in mice. Environmental

Toxicology 31(11):1430-1438. Hepatic/Liver

Health

**Outcome(s):** 

**Reported Health** Liver damage after subacute exposure to 1,2- DCE

Effect(s):

**Duration:** Short-term (>1-30 days) 10 days- Part 1, 3 concentrations

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4451633

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable	Control		
Metric 2	1: Confounding Variables in Test Design	Low	Test substance is a respiratory irritant therefore respiratory rate should be reported.
Metric 2		Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric 2	Exposure 3: Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
Metric 2	<del>-</del>	High	All outcome data were reported adequately.

# **Overall Quality Determination**

HERO ID: 4451633 Table: 3 of 3

**Study Citation:** Sun, Q., Wang, G., Gao, L., Shi, L., Qi, Y., Lv, X., Jin, Y. (2016). Roles of CYP2e1 in 1,2-dichloroethane-induced liver damage in mice. Environmental

Toxicology 31(11):1430-1438. Hepatic/Liver

Health

**Outcome(s):** 

**Reported Health** 

Liver damage after subacute exposure to 1,2- DCE

Effect(s):

Short-term (>1-30 days) 10 days- Part 2; 1 concentration **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was Shanghai Chemical Co. (Shanghai, China). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	Test substance was more than 99% pure.
Domain 2: Test Desig	rn			
	Metric 4:	Negative and Vehicle Controls	Low	Details regarding the negative control are limited and unclear if mice sham treated.
	Metric 5:	Positive Controls	N/A	Positive control was not necessary for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly divided into groups.
Domain 3: Exposure	Characterization			
Domain or Emposure	Metric 7:	Preparation and Storage of Test Substance	Low	Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored.
	Metric 8:	Consistency of Exposure	High	Exposure was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Only target concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure duration was only 3.5 hours/day (10 days).
	Metric 11:	Number of Exposure Groups and	Medium	Only one concentration was studied; concentration was justified based on effects in
	Wictie 11.	Dose/Concentration Spacing	Wicdiani	previous findings.
	Metric 12:	Exposure Route and Method	Uninformative	A static inhalation chamber was used.
Domain 4: Test Anim	als			
Domain 1. Test I iiiii	Metric 13:	Test Animal Characteristics	Medium	Age was not reported.
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.
		Husbandry Conditions		
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed /group were appropriate for the study type.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Histopathology was not performed on liver.
	Metric 17:	Consistency of Outcome Assessment	High	Details of outcome assessment protocol are adequate.
	Metric 18:	Sampling Adequacy	High	The number of animals evaluated/group was appropriate.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.

HERO ID: 4451633 Table: 3 of 3

1,1-Dichloroethane

#### ... continued from previous page

Study Citation: Sun, Q., Wang, G., Gao, L., Shi, L., Qi, Y., Lv, X., Jin, Y. (2016). Roles of CYP2e1 in 1,2-dichloroethane-induced liver damage in mice. Environmental

Toxicology 31(11):1430-1438.

Health Hepatic/Liver

**Outcome(s):** 

**Reported Health** Liver damage after subacute exposure to 1,2- DCE

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 10 days- Part 2; 1 concentration

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4451633

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable	Control		
Metric 2	1: Confounding Variables in Test Design	Low	Test substance is a respiratory irritant therefore respiratory rate should be reported.
Metric 2	and Procedures 2: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric 2	1	High	Statistical analysis was performed and appropriate.
Metric 2	4: Reporting of Data	High	All outcome data were reported adequately.

# **Overall Quality Determination**

Study Citation:	Wang, G., Qi, Y., Gao, L., Li, G., Lv, X., Jin, Y.P. (2013). Effects of subacute exposure to 1.2-dichloroethane on mouse behavior and the related mechanisms.
Study Citation.	wang, O., Oi, I., Oao, E., Ei, O., Ev, A., Jin, I.I. (2013). Effects of subacute exposure to 1,2-dictionofoculation of modes ochavior and the related mechanisms.

Human & Experimental Toxicology 32(9):983-991. Neurological/Behavioral

Health Neurological/Behaviora

**Outcome(s):** 

**Reported Health** Open field test and mechanistic endpoints

Effect(s):

**Duration:**Short-term (>1-30 days) Short-term 10 days**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was Shanghai Chemical Co. (Shanghai, China). The batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	The test substance purity was reported to be more than 99%.
Domain 2: Test Desig	gn			
•	Metric 4:	Negative and Vehicle Controls	High	Control mice were also put in the chamber for the same amount to time as exposed mice
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Medium	Mice were randomly allocated into 4 groups.
Domain 3: Exposure	Characterization			
1	Metric 7:	Preparation and Storage of Test Substance	Low	Storage and preparation of test substance were not adequately described given the volatility of test substance.
	Metric 8:	Consistency of Exposure	High	Exposure was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	Measured concentrations were reported and appropriate but target concentrations were not. This is unlikely to have a substantial impact on results.
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure to test substance was form 3.5 hours/day for 10 days, less than the recommended 6 hours/day.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Minor limitations on concentrations studied. Authors suggest a nonmonotonic response for one outcome, more concentrations would be helpful to tease this out.
	Metric 12:	Exposure Route and Method	Uninformative	The use of a static inhalation chamber, which has no airflow, is not generally acceptable for subacute inhalation toxicity studies.
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	Low	The species of mice was not reported. The animals studied were referred to as albino female mice.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were sufficiently reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed per group was appropriate (n=8).
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome methodology was appropriate for intended outcome.
		Coi	ntinued on next page .	•••

**Study Citation:** Wang, G., Qi, Y., Gao, L., Li, G., Lv, X., Jin, Y.P. (2013). Effects of subacute exposure to 1,2-dichloroethane on mouse behavior and the related mechanisms.

Human & Experimental Toxicology 32(9):983-991.

Health

Neurological/Behavioral

**Outcome(s):** 

**Reported Health** 

Open field test and mechanistic endpoints

Effect(s):

Short-term (>1-30 days) Short-term 10 days **Duration:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 1522109

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding outcome assessment were minimal but unlikely to substantially impact results.
	Metric 18:	Sampling Adequacy	High	The number of animals evaluated/group was reported (n=8).
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study because outcomes were not subjective.
	Metric 20:	Negative Control Response	High	The negative control responses were appropriate.
Domain 6: Confounding /			Low	Designation of the control of the co
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Respiratory rates were not reported. This information would be useful since the test substance is a respiratory irritant.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	High	Outcome data were reported sufficiently.

### **Overall Quality Determination**

formation induced by subacute exposure to 1,2-dichloroethane. Neurotoxicology and Teratology 44:105-112.

Wang, G., Yuan, Y., Zhang, J., Gao, L., Tan, X., Yang, G., Lv, X., Jin, Y. (2014). Roles of aquaporins and matrix metalloproteinases in mouse brain edema

HERO ID: 4453007 Table: 1 of 3

**Study Citation:** 

Health	Mortality; N	eurological/Behavioral;		2,		
Outcome(s):	Montolity, In	mont and often 2 days of averaging the montali	try mates of maios in small	and to Cavara 007 2007 and 6007 magnestively, and the live miss in arrays		
Reported Health Effect(s):	Mortality: In part one, after 3 days of exposure, the mortality rates of mice in group A to C were 0%, 30% and 60%, respectively, and the live mice ingroup B and C showed body tremors and forelimb flexure in a time dependent and dose-dependent manner. In part two, the mortality rates of mice in group D to					
Effect(s):				oned above became more severealong with the prolonged exposure time.		
				wo.; Neurological/Behavioral: Part 1: Body tremors and forelimb flexure;		
				ression of aquaporin 4, MMP2 and MMP9 in cerebral tissue;		
<b>Duration:</b>		>1-30 days) Part 1: 3 days- 3 different concen		ossion of aquaporar (, man 2 and man ) in concern assuct		
Chemical:		bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	4453007					
Domain		Metric	Rating	Comments		
Domain 1: Test Substa						
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.		
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance and/or batch/lot number were not provided.		
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was more than 99% pure.		
Domain 2: Test Design	1					
	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: Details regarding the negative control are limited and unclear if mice sham treated.		
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.		
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly divided into groups.		
Domain 3: Exposure C	Characterization					
	Metric 7:	Preparation and Storage of Test	Low	All Outcomes: Given the volatility of the test substance, the study did not adequately		
		Substance		report how test substance was prepared or stored.		
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure was administered consistently across study groups.		
	M 0	Administration	т.			
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Only target concentrations were reported.		
	Metric 10:	Exposure Frequency and Duration  Number of Exposure Groups and	Medium	All Outcomes: Exposure duration was only 3.5 hours/day.		
	Metric 11:	Dose/Concentration Spacing	High	All Outcomes: Concentrations were adequate to obtain a range of responses.		
	Metric 12:	Exposure Route and Method	Uninformative	All Outcomes: A static inhalation chamber was used.		
Domain 4: Test Anima	ıls					
	Metric 13:	Test Animal Characteristics	Medium	Mortality: Age was not reported.; Neurological/Behavioral: Age was not reported.		
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were adequately reported.		
		Husbandry Conditions	6	, x x		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed /group were appropriate for the study type (n=6).		
Domain 5: Outcome A	ssessment					
Domain 5. Outcome A	assessment	Con	ntinued on novt nogo			
		Col	ntinued on next page .	•••		

Page **486** of **955** 

Study Citation:				Roles of aquaporins and matrix metalloproteinases in mouse brain edema				
Health		formation induced by subacute exposure to 1,2-dichloroethane. Neurotoxicology and Teratology 44:105-112.  Mortality; Neurological/Behavioral;						
Outcome(s):	Mortanty, Neurological/Benavioral,							
Reported Health	Mortality: Ir	n part one after 3 days of exposure, the mortality	v rates of mice in gro	up A to C were 0%, 30% and 60%, respectively, and the live mice ingroup				
Effect(s):				e-dependent manner. In part two, the mortality rates of mice in group D to				
Effect(s).				oned above became more severealong with the prolonged exposure time.				
				two.; Neurological/Behavioral: Part 1: Body tremors and forelimb flexure;				
				pression of aquaporin 4, MMP2 and MMP9 in cerebral tissue;				
Duration:		>1-30 days) Part 1: 3 days- 3 different concent		ression of aquaporni 4, when 2 and when 9 in cerebral dissue,				
Chemical:		pethane- Isomer: 1,2-Dichloroethane	rations					
HERO ID:	4453007	retitate isomer. 1,2 Diemoroculaire						
Domain		Metric	Rating	Comments				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodology were appropriate				
	Metric 17:	Consistency of Outcome Assessment	Medium	Mortality: Details of outcome assessment protocol were limited; Neurological/Behavioral: Details of outcome assessment protocol were limited.				
	Metric 18:	Sampling Adequacy	High	All Outcomes: The number of animals evaluated/group was appropriate.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.				
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.				
Domain 6: Confound	ing / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.				
	Metric 22:	Health Outcomes Unrelated to	Medium	All Outcomes: No information was provided to either to support or dismiss differences				
		Exposure		in groups in health outcomes or attrition.				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed and appropriate.				
	Metric 24:	Reporting of Data	Medium	Mortality: Mortality data are reported for all groups but data on poisoned symptoms ar not adequately reported.; Neurological/Behavioral: Representative photos were shown for histology and observations were reported. No quantitative data was reported.				

HERO ID: 4453007 Table: 2 of 3

Study Citation:				Roles of aquaporins and matrix metalloproteinases in mouse brain edema			
IT a al4h		duced by subacute exposure to 1,2-dichloroeth	nane. Neurotoxicology	and Teratology 44:105-112.			
Health Outcome(s):	Neurologica	ii/Bellaviorai					
Reported Health	Part 1: Body tremors and forelimb flexure; brain weight, brain water content, histology of brainPart 2: RNA and protein expression of aquaporin 4, MMP2						
Effect(s):	-	in cerebral tissue	ani water content, mst	biogy of brainfart 2. KivA and protein expression of aquaporin 4, whire 2			
Duration:	Short-term (>1-30 days) Part 2: 1.2 g/m3; 2-3 days						
Chemical:		pethane- Isomer: 1,2-Dichloroethane					
HERO ID:	4453007	ethane- isomer. 1,2-Diemoroethane					
Domain		Metric	Rating	Comments			
Domain 1: Test Substar	nce						
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.			
	Metric 2:	Test Substance Source	Low	The source of the test substance and/or batch/lot number were not provided.			
	Metric 3:	Test Substance Purity	High	Test substance was more than 99% pure.			
Domain 2: Test Design							
2, 100, 200, 200, 200	Metric 4:	Negative and Vehicle Controls	Low	Details regarding the negative control are limited and unclear if mice sham treated.			
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.			
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly divided into groups.			
Domain 3: Exposure C							
	Metric 7:	Preparation and Storage of Test	Low	Given the volatility of the test substance, the study did not adequately report how test			
	M	Substance	TT' 1	substance was prepared or stored.			
	Metric 8:	Consistency of Exposure Administration	High	Exposure was administered consistently across study groups.			
	Metric 9:	Reporting of Doses/Concentrations	Low	Only target concentrations were reported.			
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure duration was only 3.5 hours/day.			
	Metric 11:	Number of Exposure Groups and	Medium	Only one concentration was studied; concentration was justified based on effects in			
		Dose/Concentration Spacing		previous findings.			
	Metric 12:	Exposure Route and Method	Uninformative	A static inhalation chamber was used.			
Domain 4: Test Animal	ls						
	Metric 13:	Test Animal Characteristics	Medium	Age was not reported.			
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.			
	3.6	Husbandry Conditions	36. "				
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed /group were appropriate for the study type (n=6).			
Domain 5: Outcome A	ssessment						
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment and methodology were appropriate			
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of outcome assessment protocol were limited			
	Metric 18:	Sampling Adequacy	High	The number of animals evaluated/group was appropriate.			
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.			
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.			
	/X/ : 11 G						
Domain 6: Confoundin	g / Variable Co	ntroi					

1,1-Dichloroethane

#### ... continued from previous page

<b>Study Citation:</b>	Wang, G., Yuan, Y., Zhang, J., Gao, L., Tan, X., Yang, G., Lv, X., Jin, Y. (2014). Roles of aquaporins and matrix metalloproteinases in mouse brain edema
	formation induced by subacute exposure to 1,2-dichloroethane. Neurotoxicology and Teratology 44:105-112.

Health

Neurological/Behavioral **Outcome(s):** 

**Reported Health** 

Part 1: Body tremors and forelimb flexure; brain weight, brain water content, histology of brainPart 2: RNA and protein expression of aquaporin 4, MMP2

HERO ID: 4453007 Table: 2 of 3

Effect(s): and MMP9 in cerebral tissue

Short-term (>1-30 days) Part 2: 1.2 g/m3; 2-3 days **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4453007

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design	Low	Test substance is a respiratory irritant therefore respiratory rate should be reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	High	Data was adequately reported.

# **Overall Quality Determination**

Wang, G., Yuan, Y., Zhang, J., Gao, L., Tan, X., Yang, G., Lv, X., Jin, Y. (2014). Roles of aquaporins and matrix metalloproteinases in mouse brain edema

HERO ID: 4453007 Table: 3 of 3

formation induced by subacute exposure to 1,2-dichloroethane. Neurotoxicology and Teratology 44:105-112.

**Study Citation:** 

Health	Mortality							
Outcome(s):								
Reported Health	In part one, after 3 days of exposure, the mortality rates of mice in group A to C were 0%, 30% and 60%, respectively, and the live mice ingroup B and C							
Effect(s):				ent manner. In part two, the mortalityrates of mice in group D to F were				
				ove became more severealong with the prolonged exposure time. There				
		abnormality in the control mice after exposure	e in part one and two.					
Duration:		>1-30 days) Part 2: 1.2 g/m3; 2-3 days						
Chemical:	· · · · · · · · · · · · · · · · · · ·	bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	4453007							
Domain		Metric	Rating	Comments				
Domain 1: Test Substa		T (0.1)	TT' 1					
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.				
	Metric 2:	Test Substance Source	Low	The source of the test substance and/or batch/lot number were not provided.				
	Metric 3:	Test Substance Purity	High	Test substance was more than 99% pure.				
Domain 2: Test Design	1							
C	Metric 4:	Negative and Vehicle Controls	Low	Details regarding the negative control are limited and unclear if mice sham treated.				
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.				
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly divided into groups.				
Domain 3: Exposure C	haracterization							
	Metric 7:	Preparation and Storage of Test	Low	Given the volatility of the test substance, the study did not adequately report how test				
		Substance		substance was prepared or stored.				
	Metric 8:	Consistency of Exposure	High	Exposure was administered consistently across study groups.				
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Only target concentrations were reported.				
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure duration was only 3.5 hours/day.				
	Metric 11:	Number of Exposure Groups and	Medium	Only one concentration was studied; concentration was justified based on effects in				
	wiedle 11.	Dose/Concentration Spacing	Wediam	previous findings.				
	Metric 12:	Exposure Route and Method	Uninformative	A static inhalation chamber was used.				
Domain 4: Test Anima	10							
Domain 4. Test Amma	Metric 13:	Test Animal Characteristics	Medium	Age of the animals was not reported.				
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.				
		Husbandry Conditions						
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed /group were appropriate for the study type (n=6).				
Domain 5: Outcome A	ssessment							
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment and methodology were appropriate				
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of outcome assessment protocol were limited				
	Metric 18:	Sampling Adequacy	High	The number of animals evaluated/group was appropriate.				
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.				
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.				
		Con		C 1 11 1				

Study Citation: Wang, G., Yuan, Y., Zhang, J., Gao, L., Tan, X., Yang, G., Lv, X., Jin, Y. (2014). Roles of aquaporins and matrix metalloproteinases in mouse brain edema

formation induced by subacute exposure to 1,2-dichloroethane. Neurotoxicology and Teratology 44:105-112.

**Health** Mortality

**Outcome(s):** 

Reported Health Effect(s):

In part one, after 3 days of exposure, the mortality rates of mice in group A to C were 0%, 30% and 60%, respectively, and the live mice ingroup B and C showed body tremors and forelimb flexure in a time dependent and dose-dependent manner. In part two, the mortality rates of mice in group D to F were 5%, 10% and 25%, respectively. The poisoned symptoms in mice mentioned above became more severealong with the prolonged exposure time. There

was not any abnormality in the control mice after exposure in part one and two.

**Duration:** Short-ten Chemical: 1,1-Dichl HERO ID: 4453007

Short-term (>1-30 days) Part 2: 1.2 g/m3; 2-3 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 6: Confounding	/ Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Low	Test substance is a respiratory irritant therefore respiratory rate should be reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	Medium	Mortality data are reported for all groups but data on poisoned symptoms are not adequately reported.

### **Overall Quality Determination**

<b>Study Citation:</b>	Zeng, N., Jiang, H., Fan, Q., Wang, T., Rong, W., Li, G., Li, R., Xu, D., Guo, T., Wang, F., Zeng, L., Huang, M., Zheng, J., Lu, F., Chen, W., Hu, Q.,
	Huang, Z., Wang, Q. (2018). Aberrant expression of miR-451a contributes to 1,2-dichloroethane-induced hepatic glycerol gluconeogenesis disorder by
	inhibiting glycerol kinase expression in NIH Swiss mice. Journal of Applied Toxicology 38(2):292-303.
TT a a l4la	NI-4-141-1-1/M-4-1-11-

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Body weight, food consumption

**Effect(s):** 

Short-term (>1-30 days) 28 days **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Test substance identified as 1,2-Dichloroethane (1,2-DCE)
Metric 2:	Test Substance Source	Low	"1,2-DCE, purchased from the Guangzhou Chemical Reagent Factory (Guangzhou, China)." The batch/lot number was not reported.
Metric 3:	Test Substance Purity	Low	Purity and/or grade of test substance were not reported
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	"Mice exposed to 28 days of filtered clean air in an inhalation chamber for 6 h day—1 for continued exposure were used as controls."
Metric 5:	Positive Controls	N/A	Not required for study type
Metric 6:	Randomized Allocation of Animals	Medium	"30 mice were randomly divided into three groups of 10 using a random number chart"
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	Low	Missing details of stability, aerosol generation method, and storage conditions."Different concentrations of 1,2-DCE solution were placed in glassware and into a standard gas generator. 1,2-DCE aerosolwas generated using a Permeacal Perimeter (PD-1B; Gastec Corp.,Ayase, Japan). 1,2-DCE aerosol connected to a dry air filter as a carrier gas in a 300 liter compressed gas cylinder was input into a whole body dynamic inhalation chamber (Guangzhou Jiufang Electronics Co., Ltd, Guangzhou, China). These chambers allowed for automatic, dynamic 50 l min—1 air recycling. The flow of gas was then controlled for exposure into the chambers"
Metric 8:	Consistency of Exposure Administration	Low	Missing information on chamber designs, animals/chamber, and particle sizes. With whole body exposure to an aerosol these factors may influence exposure.
Metric 9:	Reporting of Doses/Concentrations	High	Analytical and target chamber concentrations were reported (sampled in 1st, 3rd, and 5th hour in exposed and last hour in control groups); range within $\pm 20\%$ for liquid and solid aerosols:"The actual levels of 1,2-DCE were determined by gas chromatography—mass spectrometer, and the results showed that the concentration of 1,2-DCE in the exposure chambers during the experiment was similar to the predesigned 1,2-DCE concentrations 1,2-DCE in the air (mg m $-3$ ) among the control, 350 mg m $-3$ and 700 mg m $-3$ groups were 0.27 $\pm$ 0.11, 363.58 $\pm$ 24.76 and 731.10 $\pm$ 158.44 respectively"
Metric 10:	Exposure Frequency and Duration	High	Exposed 6 hrs/d for 28 consecutive days, standard regimen and sufficient to induce effects.
	Number of Exposure Groups and	High	2 exposure groups plus control; both NOAEL and LOAEL identified for body weight.

**Study Citation:** Zeng, N., Jiang, H., Fan, Q., Wang, T., Rong, W., Li, G., Li, R., Xu, D., Guo, T., Wang, F., Zeng, L., Huang, M., Zheng, J., Lu, F., Chen, W., Hu, Q., Huang, Z., Wang, Q. (2018). Aberrant expression of miR-451a contributes to 1,2-dichloroethane-induced hepatic glycerol gluconeogenesis disorder by inhibiting glycerol kinase expression in NIH Swiss mice. Journal of Applied Toxicology 38(2):292-303.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weight, food consumption

Effect(s):

**Duration:** Short-term (>1-30 days) 28 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Medium	Dynamic whole-body chamber was used for aerosol; air changes reported as 50 l/min but chamber volume was not reported.
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	High	"According to preliminary experimental results, male mice were more sensitive to exposure of 1,2-DCEthirty 7-week-old, male National Institutes of Health (NIH) Swiss mice (specific pathogen free, body weight 18–20 g) were purchased from the Guangdong Medical Laboratory Animal Center (Guangzhou, China)."
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	"The mice were housed in individual cages and had access to food and water ad libitum. A controlled environment at a temperature between 20 and 22°C, with a range of 50–60% humidity, and 12 hour light/dark cycle was maintained throughout the study"
	Metric 15:	Number of Animals per Group	Medium	10 animals/group; consistent with other studies of this duration
Domain 5: Outcome A	Assessment Metric 16: Metric 17: Metric 18:	Outcome Assessment Methodology Consistency of Outcome Assessment Sampling Adequacy	High High High	Body weight was measured weekly.  Body weight was measured weekly.  All animals in all groups evaluated for body weight.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for body weight measurements
	Metric 20:	Negative Control Response	High	Control response was reported and appeared appropriate
Domain 6: Confoundi	ng / Variable Coi	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Respiratory rate was not reported; 1,2-dichloroethane may be respiratory irritant.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	There were no deaths, and no health outcomes unrelated to exposure were reported.
	Metric 23:	Data Presentation and Analysis	High	"Data were expressed as a mean $\pm$ standard deviation (SD). They were analyzed by one-way analysis of variance followed by a Mann–Whitney test between groups."
	Metric 24:	Reporting of Data	High	Data were presented for all outcomes by exposure group, including mean and SD

HERO ID: 5555689 Table: 2	of 2
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Study Citation:	Zeng, N., Jiang, H., Fan, Q., Wang, T., Rong, W., Li, G., Li, R., Xu, D., Guo, T., Wang, F., Zeng, L., Huang, M., Zheng, J., Lu, F., Chen, W., Hu, Q.,
	Huang, Z., Wang, Q. (2018). Aberrant expression of miR-451a contributes to 1,2-dichloroethane-induced hepatic glycerol gluconeogenesis disorder by
	inhibiting glycerol kinase expression in NIH Swiss mice. Journal of Applied Toxicology 38(2):292-303.
Health	Hepatic/Liver

**Outcome(s):** 

**Reported Health** 

Liver weight; serum ALT, AST, glucose, triglycerides, and free fatty acids; liver glycogen, triglycerides, and free fatty acids.

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 28 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5555689

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Test substance identified as 1,2-Dichloroethane (1,2-DCE)
Metric 2:	Test Substance Source	Low	"1,2-DCE, purchased from the Guangzhou Chemical Reagent Factory (Guangzhou, China)." The batch/lot number was not reported.
Metric 3:	Test Substance Purity	Low	Purity and/or grade of test substance were not reported
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	"Mice exposed to 28 days of filtered clean air in an inhalation chamber for 6 h day-1 for continued exposure were used as controls."
Metric 5:	Positive Controls	N/A	Not required for study type
Metric 6:	Randomized Allocation of Animals	Medium	"30 mice were randomly divided into three groups of 10 using a random number chart"
Domain 3: Exposure Characterization			
. Metric 7:	Preparation and Storage of Test Substance	Low	Missing details of stability, aerosol generation method, and storage conditions."Different concentrations of 1,2-DCE solution were placed in glassware and into a standard gas generator. 1,2-DCE aerosol was generated using a Permeacal Perimeter (PD-1B; Gastec Corp.,Ayase, Japan). 1,2-DCE aerosol connected to a dry air filter as a carrier gas in a 300 liter compressed gas cylinder was input into a whole body dynamic inhalation chamber (Guangzhou Jiufang Electronics Co., Ltd, Guangzhou, China). These chambers allowed for automatic, dynamic 50 l min-1 air recycling. The flow of gas was then controlled for exposure into the chambers"
Metric 8:	Consistency of Exposure Administration	Low	Missing information on chamber designs, animals/chamber, and particle sizes. With whole body exposure to an aerosol these factors may influence exposure.
Metric 9:	Reporting of Doses/Concentrations	High	Analytical and target chamber concentrations were reported (sampled in 1st, 3rd, and 5th hour in exposed and last hour in control groups); range within $\pm 20\%$ for liquid and solid aerosols: "The actual levels of 1,2-DCE were determined by gas chromatography—mass spectrometer, and the results showed that the concentration of 1,2-DCE in the exposure chambers during the experiment was similar to the predesigned 1,2-DCE concentrations 1,2-DCE in the air (mg m $-3$ ) among the control, 350 mg m $-3$ and 700 mg m $-3$ groups were 0.27 $\pm$ 0.11, 363.58 $\pm$ 24.76 and 731.10 $\pm$ 158.44 respectively"
Metric 10:	Exposure Frequency and Duration	High	Exposed 6 hrs/d for 28 consecutive days, standard regimen and sufficient to induce effects.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	2 exposure groups plus control; effects seen at low exposure so it was not low enough to identify LOAEL.
Metric 12:	Exposure Route and Method	Medium	Dynamic whole-body chamber was used for aerosol; air changes reported as 50 l/min but chamber volume was not reported.

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Study Citation: Health	Zeng, N., Jiang, H., Fan, Q., Wang, T., Rong, W., Li, G., Li, R., Xu, D., Guo, T., Wang, F., Zeng, L., Huang, M., Zheng, J., Lu, F., Chen, W., Hu, Q. Huang, Z., Wang, Q. (2018). Aberrant expression of miR-451a contributes to 1,2-dichloroethane-induced hepatic glycerol gluconeogenesis disorder linhibiting glycerol kinase expression in NIH Swiss mice. Journal of Applied Toxicology 38(2):292-303. Hepatic/Liver							
Outcome(s):								
Reported Health Effect(s):	Liver weight	t; serum ALT, AST, glucose, triglycerides, a	and free fatty	v acids; liver glycogen, triglycerides, and free fatty acids.				
<b>Duration:</b>	Short-term (	>1-30 days) 28 days						
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	5555689							
Domain		Metric	Rating	Comments				
Domain 4: Test Anima	als							
Domain II Tool / Illinia	Metric 13:	Test Animal Characteristics	High	"According to preliminary experimental results, male mice were more sensitive to exposure of 1,2-DCEthirty 7-week-old, male National Institutes of Health (NIH) Swiss mice (specific pathogen free, body weight 18–20 g) were purchased from the Guangdong Medical Laboratory Animal Center (Guangzhou, China)."				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	"The mice were housed in individual cages and had access to food and water ad libitum. A controlled environment at a temperature between 20 and 22°C, with a range of 50–60% humidity, and 12 hour light/dark cycle was maintained throughout the study"				
	Metric 15:	Number of Animals per Group	Medium	10 animals/group; consistent with other studies of this duration				
Domain 5: Outcome A	. aaaaamant							
Domain 5: Outcome A	Metric 16:	Outcome Assessment Methodology	Medium	Hepatic endpoints included liver weight; liver concentrations of glycogen, triglycerides, and free fatty acids; and serum ALT, AST, glucose, triglycerides, and free fatty acids. Histopathology was not evaluated, decreasing sensitivity of assessment. Mechanistic endpoints consisted of liver micro-RNA profile and liver expression of Gk mRNA. Methods for all outcomes described in detail.				
	Metric 17:	Consistency of Outcome Assessment	High	All liver tissue samples obtained at sacrifice 24 hours after the last dose.				
	Metric 18:	Sampling Adequacy	Medium	All animals in all groups evaluated for hepatic endpoints; the size of liver tissue samples was not reported but results for liver contents were normalized to liver protein.				
	Metric 19:	Blinding of Assessors	N/A	Not necessary for these endpoints				
	Metric 20:	Negative Control Response	High	Control response was reported and appeared appropriate				
Domain 6: Confoundin	ng / Variable Co	ntrol						
2 omain o. Comoundi	Metric 21:	Confounding Variables in Test Design	Low	Respiratory rate was not reported; 1,2-dichloroethane may be respiratory irritant.				
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	High	There were no deaths, and no health outcomes unrelated to exposure were reported.				
	Metric 23:	Data Presentation and Analysis	High	"Data were expressed as a mean $\pm$ standard deviation (SD). They were analyzed by one-way analysis of variance followed by a Mann–Whitney test between groups."				
	Metric 24:	Reporting of Data	High	Data were presented for all outcomes by exposure group, including mean and SD and n/group.				
Overall Qual	ity Detern	nination	High					
	•		- 0					

HERO ID: 5556105 Table: 1 of 2

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Zhang, L., Jin, Y.P. (2019). Toxic effects of combined treatment of 1,2-dichloroethane and ethanol on mouse brain and the related mechanisms. Journal of **Study Citation:** Biochemical and Molecular Toxicology 33(5):1. Health Neurological/Behavioral Outcome(s): Reported Health Behavioral changes, brain weight and histopathology, oxidative stress endpoints (NPSH, MDA, SOD) in the brain, and mechanistic endpoints (mRNA and Effect(s): protein levels) in the brain. **Duration:** Short-term (>1-30 days) 3 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical: HERO ID: 5556105 Domain Metric Comments Rating Domain 1: Test Substance Metric 1: Test Substance Identity High Test substance identified as 1,2-dichloroethane (1,2-DCE) Metric 2: Test Substance Source Low source was not reported and test substance identity was NOT analytically verified Metric 3: **Test Substance Purity** Low Purity and/or grade of test substance were not reported Domain 2: Test Design Metric 4: Negative and Vehicle Controls High Control and 1,2-DCE groups that did not receive ethanol were given water by gavage on 6 consecutive days (3 days before 1,2-DCE exposure). During 1,2-DCE inhalation exposure days, controls were exposed to air for 3.5 hours each day. N/A Metric 5: Positive Controls Not required for study type Randomized Allocation of Animals Medium Metric 6: "60 mice were assigned randomly to six groups: the control group; ethanol-treated group; 1,2-DCE-intoxicated group; as well as low-, medium-, and high-dose ethanol and 1,2-DCE combined treatment groups." Authors did not describe randomization process. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low There was no mention of the method and equipment used to generate the test substance for this inhalation study. Substance Metric 8: Consistency of Exposure Low Details of exposure administration are insufficiently reported (e.g., chamber type and size, number/chamber, particle size if aerosol) and the missing information is likely to Administration have a substantial impact on results. Metric 9: Reporting of Doses/Concentrations Low Actual concentrations are not reported, it is not clear whether test substance was vapor Metric 10: **Exposure Frequency and Duration** Low Exposure frequency (3.5 hr/d) and duration (3 d) were unusual and may have been too brief to elicit an effect on brain apical endpoints. Metric 11: Number of Exposure Groups and Low Single exposure level was not high enough to elicit effect on brain apical endpoints but was high enough to induce mechanistic changes. Dose/Concentration Spacing Exposure Route and Method Metric 12: Uninformative Static chamber was used. "mice in 1,2-DCE-intoxicated group ... were exposed to 1.0 g/m3 1,2-DCE in a static exposure chamber" Domain 4: Test Animals Metric 13: Test Animal Characteristics Medium Age was not reported. "Female Kunming mice, weighing  $22 \pm 2$  g, were obtained from the Experimental Animal Laboratory of China Medical University." Metric 14: Adequacy and Consistency of Animal High "The animal room was maintained at 22°C to 24°C with a 12-hour light/dark cycle and a **Husbandry Conditions** relative humidity of 50% to 60%."

> Continued on next page ... Page **496** of **955**

# Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Zhang, L., Jin, Y.P. (2019). Toxic effects of combined treatment of 1,2-dichloroethane and ethanol on mouse brain and the related mechanisms. Journal of

Biochemical and Molecular Toxicology 33(5):1.

Health
Outcome(s):

th Neurological/Behavioral

Reported Health

Behavioral changes, brain weight and histopathology, oxidative stress endpoints (NPSH, MDA, SOD) in the brain, and mechanistic endpoints (mRNA and

**Effect(s):** protein levels) in the brain. **Duration:** Short-term (>1-30 days) 3 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5556105

Domain	Metric		Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	10/group; sufficient to detect change in mechanistic endpoints.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Sensitive endpoints were evaluated and most evaluations described: behavior, brain weight and histopathology, oxidative stress endpoints (NPSH, MDA, SOD) in the brain, and selected mechanistic mRNA and protein expression levels in the brain. Behavioral evaluation was cited to J. B. Bederson, L. H. Pitts, M. Tsuji, M. C. Nishimura, R. L. Davis, H. Bartkowski, Stroke 1986, 17(3), 472; this was not in HERO.
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment were not reported
	Metric 18:	Sampling Adequacy	Low	Numbers of animals and tissue mass/volume used for all endpoints were not reported.
	Metric 19:	Blinding of Assessors	Low	Study did not report blinding for behavioral assessments.
	Metric 20:	Negative Control Response	High	Control responses were reported and appeared as expected.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Low	respiratory rate was not reported
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	"Significant differences were evaluated by a one-way analysis of variance (ANOVA) followed by the post hoc Student-Newman-Keulstest. Joint effects were evaluated by ANOVA of with a factorial design. Statistical significance was defined as $P < 0.05$ ."
	Metric 24:	Reporting of Data	High	Data for exposure-related findings were presented for all outcomes by exposure group.

### **Overall Quality Determination**

1,1-Dichloroethane HERO ID: 5556105 Table: 2 of 2

**Study Citation:** Zhang, L., Jin, Y.P. (2019). Toxic effects of combined treatment of 1,2-dichloroethane and ethanol on mouse brain and the related mechanisms. Journal of

Biochemical and Molecular Toxicology 33(5):1.

Health

Mortality

**Outcome(s):** 

Reported Health Mortality

Effect(s):

Short-term (>1-30 days) 3 days **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Test substance identified as 1,2-dichloroethane (1,2-DCE)
	Metric 2:	Test Substance Source	Low	source was not reported and test substance identity was NOT analytically verified
	Metric 3:	Test Substance Purity	Low	Purity and/or grade of test substance were not reported
Domain 2: Test Desi	gn			
	Metric 4:	Negative and Vehicle Controls	High	Control and 1,2-DCE groups that did not receive ethanol were given water by gavage on 6 consecutive days (3 days before 1,2-DCE exposure). During 1,2-DCE inhalation exposure days, controls were exposed to air for 3.5 hours each day.
	Metric 5:	Positive Controls	N/A	Not required for study type
	Metric 6:	Randomized Allocation of Animals	Medium	"60 mice were assigned randomly to six groups: the control group; ethanol-treated group; 1,2-DCE-intoxicated group; as well as low-, medium-, and high-dose ethanol and 1,2-DCE combined treatment groups."
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	There was no mention of the method and equipment used to generate the test substance for this inhalation study.
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported (e.g., chamber type and size, number/chamber, particle size if aerosol) and the missing information is likely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Low	Actual concentrations are not reported, it is not clear whether test substance was vapor or aerosol
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure frequency (3.5 hr/d) and duration (3 d) were unusual and may have been too brief to elicit an effect on mortality
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Single exposure level was not high enough to elicit effect on mortality
	Metric 12:	Exposure Route and Method	Uninformative	Static chamber was used. "mice in 1,2-DCE-intoxicated group were exposed to 1.0 g/m3 1,2-DCE in a static exposure chamber"
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Medium	Age was not reported. "Female Kunming mice, weighing $22\pm2$ g, were obtained from the Experimental Animal Laboratory of China Medical University."
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	"The animal room was maintained at 22°C to 24°C with a 12-hour light/dark cycle and a relative humidity of 50% to 60%."
	Metric 15:	Number of Animals per Group	Medium	10/group; typical for study of this type

Study Citation: Zhang, L., Jin, Y.P. (2019). Toxic effects of combined treatment of 1,2-dichloroethane and ethanol on mouse brain and the related mechanisms. Journal of

Biochemical and Molecular Toxicology 33(5):1.

Health

Mortality

**Outcome(s):** 

Reported Health

Mortality

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 3 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5556105

Domain		Metric	Rating	Comments
Domain 5: Outcome Assess	ment			
M	Ietric 16:	Outcome Assessment Methodology	High	Mortality was assessed during study
M	letric 17:	Consistency of Outcome Assessment	Medium	Details regarding the execution of the study protocol for outcome assessment were not reported; however, observations for mortality were likely to have been performed at the same time in each group.
M	Ietric 18:	Sampling Adequacy	High	All animals evaluated for mortality
M	Ietric 19:	Blinding of Assessors	N/A	Not relevant for mortality
M	letric 20:	Negative Control Response	High	There were no control deaths.
Domain 6: Confounding / V	ariable Cor	ntrol		
M	Ietric 21:	Confounding Variables in Test Design	Low	respiratory rate was not reported
M	letric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.
M	letric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed for mortality but incidences were reported, en- abling independent analysis
M	Ietric 24:	Reporting of Data	High	Mortality rates reported by exposure group.

# **Overall Quality Determination**

HERO ID: 4453049 Table: 1 of 3

Study Citation:	Zhang, Y., Li, G., Zhong, Y., Huang, M., Wu, J., Zheng, J., Rong, W., Zeng, L., Yin, X., Lu, F., Xie, Z., Xu, D., Fan, Q., Jia, X., Wang, T., Hu, Q., Chen, W., Wang, Q., Huang, Z. (2017). 1,2-dichloroethane induces reproductive toxicity mediated by the CREM/CREB signaling pathway in male NIH Swiss mice. Toxicological Sciences 160(2):299-314.
Health	Reproductive/Developmental; Nutritional/Metabolic;
Outcome(s):	
Reported Health	Reproductive/Developmental: Testis and epididymis weight, sperm count, sperm motility, morphological analysis of spermatozoa, histology on testis and
Effect(s):	caput epididymis, apoptotic cells in testis, plasma and testis hormone levels, RNA and protein expression of enzymes and genes involved in the regulation
	and synthesis of testosterone and apoptosis; Nutritional/Metabolic: Body weight;
<b>Duration:</b>	Short-term (>1-30 days) 4 week
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**Chemical:** 1,1-Dichlor **HERO ID:** 4453049

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	Reproductive/Developmental: The source of the test substance was Guangzho (China). Batch/lot number was not provided. The structure was confirmed by NMR; Nutritional/Metabolic: The source of the test substance was Guangzho (China). Batch/lot number was not provided. The structure was confirmed by NMR.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was >99% pure.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Negative control group was included and appropriate (filtered room air).
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly divided into groups.
Damain 2. Evragava Char	o atamization			
Domain 3: Exposure Char	Metric 7:	Draparation and Starage of Test	Low	All Outcomes Civen the valetility of the test substance the study did not all most divisions.
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Target and measured concentrations with standard deviations were reported.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were reported and appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Number of concentration groups and spacing were appropriate and justification for concentrations was provided.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: A dynamic whole body inhalation chamber was used. The number of air changes/hour was not reported.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Animal characteristics were adequately reported.
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were adequately reported.
		Husbandry Conditions		
•	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed /group were appropriate for the study type.

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Study Citation:	Zhang, Y., Li, G., Zhong, Y., Huang, M., Wu, J., Zheng, J., Rong, W., Zeng, L., Yin, X., Lu, F., Xie, Z., Xu, D., Fan, Q., Jia, X., Wang, T., Hu, Q., Chen, W., Wang, Q., Huang, Z. (2017). 1,2-dichloroethane induces reproductive toxicity mediated by the CREM/CREB signaling pathway in male NIH Swiss mice. Toxicological Sciences 160(2):299-314.						
Health	Reproductive/Developmental; Nutritional/Metabolic;						
Outcome(s):							
Reported Health	Reproductive/Developmental: Testis and epididymis weight, sperm count, sperm motility, morphological analysis of spermatozoa, histology on testis and						
Effect(s):	caput epididymis, apoptotic cells in testis, plasma and testis hormone levels, RNA and protein expression of enzymes and genes involved in the regula						
	and synthesis of testosterone and apoptosis; Nutritional/Metabolic: Body weight;						
<b>Duration:</b>	Short-term (>1-30 days) 4 week						
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	4453049						
Domain		Metric	Rating	Comments			
Domain 5: Outcome A	Assessment Metric 16: Metric 17: Metric 18: Metric 19: Metric 20:	Outcome Assessment Methodology Consistency of Outcome Assessment Sampling Adequacy Blinding of Assessors Negative Control Response	High High High N/A High	All Outcomes: Outcome assessment and methodology were appropriate. All Outcomes: Outcome was assessed consistently across study groups. All Outcomes: The number of animals evaluated was adequate. All Outcomes: Blinding was not necessary for this study. All Outcomes: The negative control response was appropriate.			
Domain 6: Confoundi	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.			
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed and appropriate.			
	Metric 24:	Reporting of Data	High	All Outcomes: All outcome data were reported adequately.			
Overall Quality Determination			High				

Zhang, Y., Li, G., Zhong, Y., Huang, M., Wu, J., Zheng, J., Rong, W., Zeng, L., Yin, X., Lu, F., Xie, Z., Xu, D., Fan, Q., Jia, X., Wang, T., Hu, Q., Chen,

HERO ID: 4453049 Table: 2 of 3

**Study Citation:** 

Health R Outcome(s): Reported Health R	Reproductive	logical Sciences 160(2):299-314. //Developmental; Nutritional/Metabolic;						
Outcome(s): Reported Health		/Developmental; Nutritional/Metabolic;						
<b>Reported Health</b> R	Panroductiva							
	caput epididymis, apoptotic cells in testis, plasma and testis hormone levels, RNA and protein expression of enzymes and genes involved in the regulation and synthesis of testosterone and apoptosis; Nutritional/Metabolic: Body weight;							
	Duration: Short-term (>1-30 days) 1 week							
	*	ethane- Isomer: 1,2-Dichloroethane						
HERO ID: 4	453049							
Domain		Metric	Rating	Comments				
Domain 1: Test Substance								
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.				
N	Metric 2:	Test Substance Source	High	All Outcomes: The source of the test substance was Guangzho (China). Batch/lot number was not provided. The structure was confirmed by NMR				
N	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was >99% pure.				
Danisia 2. Tark Darian								
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Negative control group was included and appropriate (filtered room air).				
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.				
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly divided into groups.				
10	vieure o.	Randonnized Anocation of Animais	Medium	All Outcomes. Animals were randomly divided into groups.				
Domain 3: Exposure Chara	cterization							
N	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored.				
N	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure was administered consistently across study groups.				
N	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	All Outcomes: Measured concentrations were not reported (they were reported for the 4 week study). This is unlikely to have a substantial impact on results.				
N	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were reported and appropriate.				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Number of concentration groups and spacing were appropriate and justification for concentrations was provided.				
N	Metric 12:	Exposure Route and Method	Medium	All Outcomes: A dynamic whole body inhalation chamber was used. The number of air changes/hour was not reported.				
Domain 4: Test Animals								
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Animal characteristics were adequately reported.				
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were adequately reported.				
14		Husbandry Conditions	6					
N	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed /group were appropriate for the study type.				
Domain 5: Outcome Assess	ement							
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodology were appropriate.				
		Contir	nued on nex	rt nage				

<b>Study Citation:</b>	Zhang, Y., Li, G., Zhong, Y., Huang, M., Wu, J., Zheng, J., Rong, W., Zeng, L., Yin, X., Lu, F., Xie, Z., Xu, D., Fan, Q., Jia, X., Wang, T., Hu, Q., Chen, W., Wang, Q., Huang, Z. (2017). 1,2-dichloroethane induces reproductive toxicity mediated by the CREM/CREB signaling pathway in male NIH Swiss							
	mice. Toxicological Sciences 160(2):299-314.							
Health	Reproductive/Developmental; Nutritional/Metabolic;							
Outcome(s):	Toploducule, 20 letophicului, 1 luulivoluu 110moolie,							
Reported Health	Reproductive/Developmental: Testis and epididymis weight, sperm count, sperm motility, morphological analysis of spermatozoa, histology on testis and							
Effect(s):	-	caput epididymis, apoptotic cells in testis, plasma and testis hormone levels, RNA and protein expression of enzymes and genes involved in the regulation						
Lifect(b).	and synthesis of testosterone and apoptosis; Nutritional/Metabolic: Body weight;							
Duration:	Short-term (>1-30 days) 1 week							
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane							
HERO ID:	4453049							
Domain		Metric	Rating	Comments				
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome was assessed consistently across study groups.				
	Metric 18:	Sampling Adequacy	High	All Outcomes: The number of animals evaluated was adequate.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.				
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.				
Damain & Canfayadi	na / Variabla Car	stual						
Domain 6: Confoundi			I					
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.				
	Metric 22:	Health Outcomes Unrelated to	Medium	All Outcomes: No information was provided to either to support or dismiss differences				
		Exposure		in groups in health outcomes or attrition.				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed and appropriate.				
	Metric 24:	Reporting of Data	High	All Outcomes: All outcome data were reported adequately.				
Overall Quality Determination			High					

HERO ID: 4453049 Table: 3 of 3

**Study Citation:** Zhang, Y., Li, G., Zhong, Y., Huang, M., Wu, J., Zheng, J., Rong, W., Zeng, L., Yin, X., Lu, F., Xie, Z., Xu, D., Fan, Q., Jia, X., Wang, T., Hu, Q., Chen, W., Wang, Q., Huang, Z. (2017). 1,2-dichloroethane induces reproductive toxicity mediated by the CREM/CREB signaling pathway in male NIH Swiss mice. Toxicological Sciences 160(2):299-314. Health Genotoxicity (Genotoxicity); Genotoxicity (Genotoxicity); Outcome(s): Reported Health Genotoxicity (Genotoxicity): Comet assay on spermatozoa; Genotoxicity (Genotoxicity): Comet assay on spermatozoa; Effect(s): **Duration:** Short-term (>1-30 days) 1 week Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 4453049 Rating Domain Metric Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: Test substance was identified as 1,2-dichloroethane. Metric 2: Test Substance Source High All Outcomes: The source of the test substance was Guangzho (China). Batch/lot number was not provided. The structure was confirmed by NMR Metric 3: Test Substance Purity High All Outcomes: Test substance was >99% pure. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: Negative control group was included and appropriate (filtered room air). Metric 5: Positive Controls Uninformative All Outcomes: Positive control was not included. Study reports negative findings in the genotoxicity assay. Authors do not report that the laboratory has performed this assay in the past. Metric 6: Randomized Allocation of Animals Medium All Outcomes: Animals were randomly divided into groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low All Outcomes: Given the volatility of the test substance, the study did not adequately report how test substance was prepared or stored. Substance Metric 8: Consistency of Exposure High All Outcomes: Exposure was administered consistently across study groups. Administration Reporting of Doses/Concentrations Metric 9: High All Outcomes: Target and measured concentrations with standard deviations were reported. Metric 10: Exposure Frequency and Duration High All Outcomes: Exposure frequency and duration were reported and appropriate. Number of Exposure Groups and Metric 11: High All Outcomes: Number of concentration groups and spacing were appropriate and justi-Dose/Concentration Spacing fication for concentrations was provided. Metric 12: Exposure Route and Method Medium All Outcomes: A dynamic whole body inhalation chamber was used. The number of air changes/hour was not reported. Domain 4: Test Animals Metric 13: Test Animal Characteristics High All Outcomes: Animal characteristics were adequately reported. Metric 14: Adequacy and Consistency of Animal High All Outcomes: Husbandry conditions were adequately reported. **Husbandry Conditions** Metric 15: Number of Animals per Group Medium All Outcomes: The number of animals exposed /group were appropriate for the study type. Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology High All Outcomes: Outcome assessment and methodology were appropriate. Continued on next page ...

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Study Citation:	Zhang, Y., Li, G., Zhong, Y., Huang, M., Wu, J., Zheng, J., Rong, W., Zeng, L., Yin, X., Lu, F., Xie, Z., Xu, D., Fan, Q., Jia, X., Wang, T., Hu, Q., Chen,
Study Citation.	
	W., Wang, Q., Huang, Z. (2017). 1,2-dichloroethane induces reproductive toxicity mediated by the CREM/CREB signaling pathway in male NIH Swiss
	mice. Toxicological Sciences 160(2):299-314.
Health	Genotoxicity (Genotoxicity); Genotoxicity (Genotoxicity);
Outcome(s):	
Departed Health	Constantiate (Constantiate), Compt again on anomatoria Constantiate (Constantiate), Compt again on anomatoria

**Reported Health** Genotoxicity (Genotoxicity): Comet assay on spermatozoa; Genotoxicity (Genotoxicity): Comet assay on spermatozoa;

**Effect(s):** 

**Duration:** Short-term (>1-30 days) 1 week

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4453049

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome was assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: The number of animals evaluated was adequate.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.
Domain 6: Confound	ing / Variable Co Metric 21:	ntrol Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	High	All Outcomes: All outcome data were reported adequately.

# **Overall Quality Determination**

# Uninformative

Study Citation:	Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). T	Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and
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Cosmetics Toxicology 14(2):105-111. Nutritional/Metabolic; Nutritional/Metabolic; Health

**Outcome(s):** 

**Reported Health** Nutritional/Metabolic: body weight, food consumption; Nutritional/Metabolic: body weight, food consumption;

Effect(s):

**Duration:** Subchronic (>30-91 days) 5 wk (growth exp females) Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test chemical was reported by name as ethylene dichloride (1,2 dichloroethane). CASRN was not reported.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was not reported; however, it was analytically verified by the laboratory.
	Metric 3:	Test Substance Purity	Low	All Outcomes: Purity of test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study included concurrent negative controls (implied unfumigated diet) and conditions were not explicitly stated, but assumed to be consistent with the treated animals.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: There were no reported details on allocation or distribution of animals.
Domain 3: Exposure Cl	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The test substance preparation was as follows: feed was exposed to the test substance in hermetically sealed containers and stored in polyvinyl bags coated in polyamide or sealed hermetically in glass jars with a polyamide layered plastic lid. The fumigated feed was stored for a maximum storage duration of 10 days during which loss was analyzed to be approximately 5%.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: The test substance was administered via fumigated diet. Feed mash was administered for a limited period (1 or 2 hours) twice a day at the same time each day. Consumption and concentration of the test substance was measured in effort to maintain consistency. It was not reported whether animals were trained to the limited feeding schedule prior to implementation.
-		Cont	inued on next ne	

**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111. Nutritional/Metabolic; Nutritional/Metabolic;

**Outcome(s):** 

Health

**Reported Health** Effect(s):

Nutritional/Metabolic: body weight, food consumption; Nutritional/Metabolic: body weight, food consumption;

**Duration:** Subchronic (>30-91 days) 5 wk (growth exp females) 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

HERO ID:	194588			
Domain		Metric	Rating	Comments
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Administered diet concentration (ppm) were reported. Diet was weighed (weekly) in order to determine amount consumed but those results were not reported. Feed was consumed primarily in the evening time frame with the majority during the first hour indicating the dose was consumed largely in a small time frame. Doses present in the diet after the 1-2h consumption period were reportedly 60-70% that of initially in mash and the authors stated, "since the amount eaten and the residue level were known, the amount of fumigant actually consumed was calculated with fair accuracy", therefore it is implied that this was accounted for. It is unclear if the introduction of diet for limited time frames caused any initial changes in food consumption, thus altering the dose consumed, though the authors reported the animals "grew accustomed to consuming it quickly". It is unclear if the amount consumed is consistent to that consumed if feed were presented ad libitum. The doses could potentially be calculated.
	Metric 10:	Exposure Frequency and Duration	Medium	Nutritional/Metabolic: Animals were administered the test substance in the diet twice daily for 1 hour in the day and 2 hours in the evening, for 7 days/week. This exposure frequency differs from typical study design but was altered due to test substance volatility. Exposure duration was 6 weeks and less than recommended, but appropriate for the study type.; Nutritional/Metabolic: Animals were administered the test substance in the diet twice daily for 1 hour in the day and 2 hours in the evening, for 7 days/week. This exposure frequency differs from typical study design but was altered due to test substance volatility. Exposure duration was 13 weeks and appropriate for the study type.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The number of exposure groups was limited to 2 treated groups and a control. Dose spacing did not encompass any effects therefore it is unclear whether spacing was appropriate.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The exposure method was not suited to the test substance. The test substance is volatile, and it was prepared in the diet. However, the authors attempted to mitigate the issues of volatility in feed via sealed fumigation, limited feeding times and monitoring of the test substance residues.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Nutritional/Metabolic: Animal characteristics were not completely reported. The details included the species (rats) and sex (female). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.; Nutritional/Metabolic: Animal characteristics were not completely reported. The details included the species (rats) and sex (male). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.

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Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health
Outcome(s):

Nutritional/Metabolic; Nutritional/Metabolic;

Reported Health

Nutritional/Metabolic: body weight, food consumption; Nutritional/Metabolic: body weight, food consumption;

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 5 wk (growth exp females) **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

HERO ID.	174300			
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry conditions were not sufficiently reported to evaluate adequacy.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals (18/group) were reported and were adequate for this study type.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Animals were weighed weekly. The outcome assessment was sensitive and appropriate for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The outcome assessment was briefly described and was carried out consistently across groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: While not explicitly reported, it was assumed all animals were sampled for the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary because this outcome of interest is not subjective in nature or is not required for this outcome of interest.
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control animals responded appropriately.
Domain 6: Confound	ding / Variable Co	ntrol		
Domain of Comount	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Information to determine confounding was not reported. No differences were identified from the reported information. With the measured residue of the test substance being 60-70% in feed after the feeding period (of 1-2 hours) it is possible that due to the volatility of the test substance, some was inhaled. Information regarding food consumption was insufficient so it is unclear whether the animals consumed an amount similar to that of feed presented ad libitum. It is unclear whether there were palatability issues (if there were, they may have been complicated by the intermittent feeding).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no reported information either to support or dismiss any differences among groups that would influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were used and reported as analysis of variance with Duncan multiple range test pairwise comparison. Significance was denoted in tables and figures. This is an appropriate method of analysis for the data type.
	Metric 24:	Reporting of Data	Medium	All Outcomes: The study data were reported in a table for each group and discussed in the text.

# **Overall Quality Determination**

# Medium

HERO ID: 194588 Table: 2 of 2

**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111. Health Hepatic/Liver Outcome(s): Reported Health liver fat content, serum total protein, cholesterol, ALT, AST Effect(s): **Duration:** Subchronic (>30-91 days) 5-7 wk (preliminary study) Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane HERO ID: 194588 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High The test chemical was reported by name as ethylene dichloride (1,2 dichloroethane). CASRN was not reported. Metric 2: Test Substance Source High The test substance source was not reported; however, it was analytically verified by the laboratory. Metric 3: Test Substance Purity Low Purity of test substance was not reported. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High The study included concurrent negative controls (implied unfumigated diet) and conditions were not explicitly stated, but assumed to be consistent with the treated animals. Metric 5: Positive Controls N/A Positive controls are not required for this study type. Metric 6: Randomized Allocation of Animals Low There were no reported details on allocation or distribution of animals. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium The test substance preparation was as follows: feed was exposed to the test substance in hermetically sealed containers and stored in polyvinyl bags coated in polyamide or Substance sealed hermetically in glass jars with a polyamide layered plastic lid. The fumigated feed was stored for a maximum storage duration of 10 days during which loss was analyzed to be approximately 5%. Metric 8: Consistency of Exposure Medium The test substance was administered via fumigated diet. Feed mash was administered for a limited period (1 or 2 hours) twice a day at the same time each day. Consumption Administration and concentration of the test substance was measured in effort to maintain consistency. It was not reported whether animals were trained to the limited feeding schedule prior to implementation. Metric 9: Reporting of Doses/Concentrations Medium Administered diet concentration (ppm) were reported. Diet was weighed (weekly) in order to determine amount consumed but those results were not reported. Feed was consumed primarily in the evening time frame with the majority during the first hour indicating the dose was consumed largely in a small time frame. Doses present in the diet after the 1-2h consumption period were reportedly 60-70% that of initially in mash and the authors stated, "since the amount eaten and the residue level were known, the amount of fumigant actually consumed was calculated with fair accuracy", therefore, it is implied that this was accounted for. It is unclear if the introduction of diet for limited time frames caused any initial changes in food consumption, thus altering the dose consumed, though the authors reported the animals "grew accustomed to consuming

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it quickly". It is unclear if the amount consumed is consistent to that consumed if feed

were presented ad libitum. The doses could potentially be calculated.

HERO ID: 194588 Table: 2 of 2

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Study Citation:	Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and
	Cosmetics Toxicology 14(2):105-111.
Health	Hepatic/Liver

Health

**Outcome(s):** 

Reported Health

liver fat content, serum total protein, cholesterol, ALT, AST

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 5-7 wk (preliminary study) **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were administered the test substance in the diet twice daily for 1 hour in the day and 2 hours in the evening, for 7 days/week. This exposure frequency differs from typical study design but was altered due to test substance volatility. Exposure duration was 5-7 weeks and appropriate for the study type.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of groups included 3 treated groups and a control and was therefore appropriate for the study. However, the low and mid dose groups were compared with a separate control in trial one, whereas the high dose group was compared with another control group during a second trial. The dose spacing was sufficient as no effects were observed at the low and mid doses and effects were observed at the high dose.
	Metric 12:	Exposure Route and Method	Medium	The exposure method was not suited to the test substance. The test substance is volatile, and it was prepared in the diet. However, the authors attempted to mitigate the issues of volatility in feed via sealed fumigation, limited feeding times and monitoring of the test substance residues.
Domain 4: Test Animals	1			
Domain Trest Immus	Metric 13:	Test Animal Characteristics	Medium	Animal characteristics were not completely reported. The details included the species (rats). Strain, age, sex and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not sufficiently reported to evaluate adequacy.
	Metric 15:	Number of Animals per Group	Medium	The number of animals (6/group) were reported and were adequate for this study type.
Domain 5: Outcome Ass	sessment			
Bonian 3. Gueome Asi	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment included liver weights, and liver lipids. The assessment did not include serum chemistry or liver histology. The assessment was sensitive but only partially addressed the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The outcome assessment was briefly described, previously cited and was carried out consistently across groups.
	Metric 18:	Sampling Adequacy	High	In table 1 it was reported that all animals were sampled for the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary because this outcome of interest is not subjective in nature or is not required for this outcome of interest.
	Metric 20:	Negative Control Response	High	Negative control animals responded appropriately.

Domain 6: Confounding / Variable Control

HERO ID: 194588 Table: 2 of 2

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**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Hepatic/Liver

**Outcome(s):** 

**Reported Health** 

liver fat content, serum total protein, cholesterol, ALT, AST

Effect(s):

Subchronic (>30-91 days) 5-7 wk (preliminary study) **Duration: Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Information to determine confounding was not reported. No differences were identified from the reported information. With the measured residue of the test substance being 60-70% in feed after the feeding period (of 1-2 hours) it is possible that due to the volatility of the test substance, some was inhaled. Information regarding food consumption was insufficient so it is unclear whether the animals consumed an amount similar to that of feed presented ad libitum. It is unclear whether there were palatability issues (if there were, they may have been complicated by the intermittent feeding).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no reported information either to support or dismiss any differences among groups that would influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical methods were used and reported as analysis of variance with Duncan multiple range test. However as two separate trials were performed (trial 1 compared a control with the low and mid doses, whereas, in trial 2, the high dose group was compared with a separate control group), it is unclear whether the test was appropriate.
	Metric 24:	Reporting of Data	Medium	The study data were reported in a table for each group but not by sex. Results were discussed in the text.

# **Overall Quality Determination**

# Medium

Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley

HERO ID: 62965 Table: 1 of 4

**Study Citation:** 

Health Outcome(s): Reported Health Effect(s):  Duration: Chemical: HERO ID:	rats. Drug and Chemical Toxicology 17(4):463-477. Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; 'other' target organ (Adrenal glands, pancreas, parathyroid); Renal/Kidney; Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Lung/Respiratory: Organ weight (lungs), gross (lungs), histopathology (lungs, nasal cavity/turbinates); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day onl differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenter nodes, thymus); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (bratitional/Metabolic: Body weights, food consumption, water consumption; Reproductive/Developmental: Organ weight (ovaries, testes), gross (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Missing 'other' targ (Adrenal glands, pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, para Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Subchronic (>30-91 days) 90 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
Domain		Metric	Rating	Comments			
Domain 1: Test Substan							
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as "1,2-dichloroethane" and synonym "ethylene dichloride." The CASRN was listed as "100706-2" instead of 107-06-2, but this is assumed to be a typo.			
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from a commercial supplier.			
	Metric 3:	Test Substance Purity	Medium	All Outcomes: It was noted that the purity of the test substance was verified by GCMS and no impurities were found; however, the numerical purity was not reported. Although the purity was not reported, this metric is rated as Medium because no impurities were found.			
Domain 2: Test Design							
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Corn oil vehicle controls were included.			
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.			
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: It was specified that animals were randomly allocated to vehicle and control groups.			
Domain 3: Exposure Ch	naracterization						
_	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The test substance is volatile and was mixed fresh daily.			
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance administration appeared to be consistent across study groups and gavage volume was not excessive (0.1 mL/ 100g bw).			
	3.5	D ' CD 'C	TT' 1				

High

High

Continued on next page ...

All Outcomes: Doses were reported without ambiguity.

purpose of the study.

All Outcomes: The exposure frequency and duration were appropriate for the intended

Reporting of Doses/Concentrations

**Exposure Frequency and Duration** 

Metric 9:

Metric 10:

			lueu Iroin p	10			
Study Citation:	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley						
Health	rats. Drug and Chemical Toxicology 17(4):463-477.  Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; Missing						
Outcome(s):		t organ (Adrenal glands, pancreas, parathyro	•				
Reported Health							
Effect(s):  Duration: Chemical: HERO ID:	Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Lung/Respiratory: Organ weight (lungs), gross necropsy (lungs), histopathology (lungs, nasal cavity/turbinates); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lympinodes, thymus); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain), histopathology (brain), histopathology (brain), mutritional/Metabolic: Body weights, food consumption, water consumption; Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Missing 'other' target orga (Adrenal glands, pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubing [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Subchronic (>30-91 days) 90 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
Domain	62965	Metric	Rating	Comments			
2 2	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The rationale for the 90-day study was not specifically stated, but the 10-day study showed excessive mortality at the highest dose, 300 mg/kg/day, which was chosen because it was approximately 44% the LD50. The highest dose in the 90-day study was reduced in comparison (150 mg/kg/day).			
	Metric 12:	Exposure Route and Method	High	All Outcomes: The oral route was appropriate for the test substance and study type.			
Domain 4: Test Animals	;						
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Starting body weight was not reported, but the remaining characteristics were reported and appropriate. Animals were obtained from a commercial source.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: It was reported that animals were housed in a temperature- and humidity-controlled room, but the temperature and humidity were not reported. Remaining animal husbandry parameters were reported and appropriate.			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: There were 10 animals/sex/group, which is considered appropriate for the 90-day study.			
Domain 5: Outcome Ass	sessment						

... continued from previous page **Study Citation:** Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477. Health Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; Missing Outcome(s): 'other' target organ (Adrenal glands, pancreas, parathyroid); Renal/Kidney; Reported Health Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Lung/Respiratory: Organ weight (lungs), gross necropsy Effect(s): (lungs), histopathology (lungs, nasal cavity/turbinates); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption; Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); **Duration:** Subchronic (>30-91 days) 90 days Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 62965 Domain Metric Rating Comments Metric 16: Outcome Assessment Methodology High Cardiovascular: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, and gross necropsy) were reported and appropriate for the outcome of interest.; Lung/Respiratory: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, and gross necropsy) were reported and appropriate for the outcome of interest.; Immune/Hematological: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy, and blood sampling after overnight fasting) were reported and appropriate for the outcome of interest.; Neurological/Behavioral: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy, and daily cageside observations) were reported and appropriate for the outcome of interest.; Nutritional/Metabolic: The assessment methodologies were appropriate for the outcomes of interest. Body weights were determined on days 4, 8 and at necropsy. Food and water consumption were measured twice weekly.; Reproductive/Developmental: The assessment methodologies (histopathology conducted by a

### Continued on next page ...

for the outcome of interest.

veterinary pathologist, organ weights, and gross necropsy) were reported and appropriate for the outcome of interest.; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy after overnight fasting) were reported and appropriate for the outcome of interest.; Renal/Kidney: The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy, urine sampling, blood sampling after overnight fasting) were reported and appropriate

**Study Citation:** Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477. Health Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; Missing **Outcome(s):** 'other' target organ (Adrenal glands, pancreas, parathyroid); Renal/Kidney; **Reported Health** Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Lung/Respiratory: Organ weight (lungs), gross necropsy Effect(s): (lungs), histopathology (lungs, nasal cavity/turbinates); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption; Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); **Duration:** Subchronic (>30-91 days) 90 days

Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 

62965

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Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	High	Cardiovascular: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Lung/Respiratory: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Immune/Hematological: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Neurological/Behavioral: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice. For cageside observations, "all rats were observed daily for physiological and behavioral responses as well as mortality."; Nutritional/Metabolic: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided.; Reproductive/Developmental: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice:; Renal/Kidney: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was as
	Metric 18:	Sampling Adequacy	High	All Outcomes: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: No subjective measurements were assessed. Blinding is not required for initial histopathology review.
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were adequate.

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Study Citation: Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477.

Health
Outcome(s):
Reported Health
Effect(s):

Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Renal/Kidney;

Cardiovascular: Organ weight (heart), gross necropsy (heart, aorta), histopathology (heart, aorta); Lung/Respiratory: Organ weight (lungs), gross necropsy (lungs), histopathology (lungs, nasal cavity/turbinates); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBC differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymph nodes, thymus); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain); Nutritional/Metabolic: Body weights, food consumption, water consumption; Reproductive/Developmental: Organ weight (ovaries, testes), gross necropsy (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, parathyroid); Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total bilirubin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder);

**Duration:** Subchronic (>30-91 days) 90 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62965

HERO ID.	02903			
Domain		Metric	Rating	Comments
Domain 6: Confounding	y / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: The study protocol was well-described and no potentially confounding factors were identified.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: No health outcomes unrelated to exposure were identified that could influence the assessment.
	Metric 23:	Data Presentation and Analysis	High	Cardiovascular: Statistical analysis is reported and appropriate for organ weight data. Statistical analysis is not necessary for gross necropsy and histopathological examination because no findings were observed for cardiac samples (negative data).; Lung/Respiratory: Statistical analysis is reported and appropriate for organ weight data. Statistical analysis is not necessary for gross necropsy and histopathological examination because no findings were observed for lung/respiratory organ samples (negative data).; Immune/Hematological: Statistical analysis is reported and appropriate for hematology, clinical chemistry, and organ weight data. Statistical analysis is not necessary for gross necropsy or histopathological examination data because no findings were observed for these assays (negative data).; Neurological/Behavioral: Statistical analysis is reported and appropriate for organ weight data. Statistical analysis is not necessary for gross necropsy, histopathological examination, or clinical signs data because no findings were observed for these assays (negative data).; Nutritional/Metabolic: Statistical analysis is reported and appropriate for body weight, food consumption, water consumption, clinical chemistry, and organ weight data.; Reproductive/Developmental: Statistical analysis is reported and appropriate for organ weight data. Statistical analysis is not necessary for gross necropsy and histopathological examination because no findings were observed for reproductive organ samples (negative data).; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Statistical analysis is reported and appropriate for organ weight data. No statistical analysis was conducted on the gross necropsy or histopathology data and no incidence information is provided; however, statistical analysis is not necessary because no findings were observed for these endpoints (negative data).; Renal/Kidney: Statistical analysis is reported and appropriate for clinical chemistry and organ weight data. No statistical a

HERO ID: 62965 Table: 1 of 4

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rats. Drug and Chemical Toxicology 17(4):463 Cardiovascular; Lung/Respiratory; Immune/ 'other' target organ (Adrenal glands, pancreas, Cardiovascular: Organ weight (heart), gross ne (lungs), histopathology (lungs, nasal cavity/tur differentials [90-day only]), organ weight (spl nodes, thymus); Neurological/Behavioral: Phy tritional/Metabolic: Body weights, food consu	8-477. Hematological; Neu parathyroid); Renal/cropsy (heart, aorta), binates); Immune/Heen, thymus), gross/siological/behaviora	histopathology (heart, aorta); Lung/Respiratory: Organ weight (lungs), gross necrops ematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBo necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymp		
'other' target organ (Adrenal glands, pancreas, Cardiovascular: Organ weight (heart), gross ne (lungs), histopathology (lungs, nasal cavity/tur differentials [90-day only]), organ weight (spl nodes, thymus); Neurological/Behavioral: Phy tritional/Metabolic: Body weights, food consu	parathyroid); Renal/cropsy (heart, aorta), binates); Immune/Heen, thymus), gross/siological/behaviora	/Kidney; histopathology (heart, aorta); Lung/Respiratory: Organ weight (lungs), gross necrops ematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBo necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymp		
Cardiovascular: Organ weight (heart), gross ne (lungs), histopathology (lungs, nasal cavity/tur differentials [90-day only]), organ weight (spl nodes, thymus); Neurological/Behavioral: Phy tritional/Metabolic: Body weights, food consu	cropsy (heart, aorta), binates); Immune/Ho een, thymus), gross vsiological/behaviora	histopathology (heart, aorta); Lung/Respiratory: Organ weight (lungs), gross necrops ematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBo necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymp		
(lungs), histopathology (lungs, nasal cavity/tur differentials [90-day only]), organ weight (spl nodes, thymus); Neurological/Behavioral: Phy tritional/Metabolic: Body weights, food consu	binates); Immune/Hoeen, thymus), gross vsiological/behaviora	ematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only], WBo necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenteric lymp		
(lungs), histopathology (lungs, nasal cavity/turbinates); Immune/Hematological: Hematology (WBC, RBC, Hgb, Hct, platelet count [90-day only differentials [90-day only]), organ weight (spleen, thymus), gross necropsy (spleen, thymus), histopathology (spleen, mandibular and mesenter nodes, thymus); Neurological/Behavioral: Physiological/behavioral responses, organ weight (brain), gross necropsy (brain), histopathology (brain), histopathology (brain), histopathology (brain), histopathology (brain), histopathology (gonads), histopathology (gonads, seminal vesicles, prostate, uterus, pituitary, preputial or clitoral gland, mammary gland); Missing 'other' targ (Adrenal glands, pancreas, parathyroid): Organ weights (adrenals), gross necropsy (adrenal glands), histopathology (adrenals, pancreas, para Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilinogen, occult blood) [90-day only], clinical chemistry (BUN, creatinine, total [90-day only]), organ weight (kidneys), gross necropsy (kidneys), histopathology (kidneys, urinary bladder); Subchronic (>30-91 days) 90 days				
62965				
Metric	Rating	Comments		
Metric 24: Reporting of Data	High	Cardiovascular: Negative findings were reported qualitatively (gross pathology and histopathology) or quantitatively (organ weight).; Lung/Respiratory: Negative findings were reported qualitatively (gross pathology, histopathology) or quantitatively (lung weight).; Immune/Hematological: All data were reported adequately. Negative findings were reported qualitatively (gross pathology, histopathology) or quantitatively (organ weight, hematology).; Neurological/Behavioral: Negative findings were reported qualitatively or quantitatively.; Nutritional/Metabolic: All data were reported adequately. Negative findings were reported qualitatively (food and water consumption) or quantitatively (body weight).; Reproductive/Developmental: Negative findings were reported qualitatively (gross pathology, histopathology) or quantitatively (testes, ovaries).; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid): Negative data is adequately presented qualitatively (gross pathology, histopathology) or quantitatively (adrenal weight); Renal/Kidney: All data were reported adequately. Negative findings were reported qualitatively or quantitatively.		
	(Adrenal glands, pancreas, parathyroid): Org Renal/Kidney: Urinalysis (pH, protein, glucos [90-day only]), organ weight (kidneys), gross r Subchronic (>30-91 days) 90 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethan 62965	(Adrenal glands, pancreas, parathyroid): Organ weights (adrenals Renal/Kidney: Urinalysis (pH, protein, glucose, bilirubin, urobilin [90-day only]), organ weight (kidneys), gross necropsy (kidneys), f Subchronic (>30-91 days) 90 days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 62965  Metric Rating		

**Study Citation:** Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477. Hepatic/Liver Health **Outcome(s): Reported Health** Clinical chemistry (ALP, AST, ALT, cholesterol [10-day only]), organ weight (liver), gross necropsy (liver), histopathology (liver) Effect(s):

Subchronic (>30-91 days) 90 days **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62965

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as "1,2-dichloroethane" and synonym "ethylene dichloride." The CASRN was listed as "100706-2" instead of 107-06-2, but this is assumed to be a typo.
	Metric 2:	Test Substance Source	High	The test substance was obtained from a commercial supplier.
	Metric 3:	Test Substance Purity	Medium	It was noted that the purity of the test substance was verified by GCMS and no impurities were found; however, the numerical purity was not reported. Although the purity was not reported, this metric is rated as Medium because no impurities were found.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Corn oil vehicle controls were included.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	It was specified that animals were randomly allocated to vehicle and control groups.
Domain 3: Exposure C				
	Metric 7:	Preparation and Storage of Test	High	The test substance is volatile and was mixed fresh daily.
	Metric 8:	Substance Consistency of Exposure Administration	High	Test substance administration appeared to be consistent across study groups and gavage volume was not excessive (0.1 mL/ 100g bw).
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for the intended purpose of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The rationale for the 90-day study was not specifically stated, but the 10-day study showed excessive mortality at the highest dose, 300 mg/kg/day, which was chosen because it was approximately 44% the LD50. The highest dose in the 90-day study was reduced in comparison (150 mg/kg/day).
	Metric 12:	Exposure Route and Method	High	The oral route was appropriate for the test substance and study type.
Domain 4: Test Animal				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weight was not reported, but the remaining characteristics were reported and appropriate. Animals were obtained from a commercial source.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	It was reported that animals were housed in a temperature- and humidity-controlled room, but the temperature and humidity were not reported. Remaining animal husbandry parameters were reported and appropriate.

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Study Citation:	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawler rats. Drug and Chemical Toxicology 17(4):463-477.							
Health	Hepatic/Live							
Outcome(s):								
Reported Health	Clinical chemistry (ALP, AST, ALT, cholesterol [10-day only]), organ weight (liver), gross necropsy (liver), histopathology (liver)							
Effect(s):								
Duration:	Subchronic (>30-91 days) 90 days							
Chemical:		bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	62965							
Domain		Metric	Rating	Comments				
Domain 5: Outcome A	Assessment							
	Metric 16:	Outcome Assessment Methodology	High	The assessment methodologies (histopathology conducted by a veterinary pathologist, organ weights, gross necropsy, and blood sampling after overnight fasting) were reported and appropriate for the outcome of interest.				
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. For histopathological examination, only the highest dose group was assessed initially, which is standard practice.				
	Metric 18:	Sampling Adequacy	High	All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.				
	Metric 19:	Blinding of Assessors	N/A	No subjective measurements were assessed. Blinding is not required for initial histopathology review.				
	Metric 20:	Negative Control Response	High	The negative control responses were adequate.				
Domain 6: Confoundi	ng / Variable Cor	ntrol						
Domain of Comounds	Metric 21:	Confounding Variables in Test Design and Procedures	High	The study protocol was well-described and no potentially confounding factors were identified.				
	Metric 22:	Health Outcomes Unrelated to Exposure	High	No health outcomes unrelated to exposure were identified that could influence the assessment.				
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis is reported and appropriate for clinical chemistry and organ weight data. No statistical analysis was conducted on the gross necropsy and histopathology data and no incidence information is provided; however, statistical analysis is not necessary because the study focused on pathology findings.				
	Metric 24:	Reporting of Data	Medium	Negative findings were reported qualitatively (gross pathology, histopathology) or quantitatively (relative liver weight). ALP was reported to be increased in males of the two highest treatment groups; however, the data supporting this change is not shown, nor is the magnitude of the effect described qualitatively in the text.				

<b>Study Citation:</b>	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley
	rats. Drug and Chemical Toxicology 17(4):463-477.

**Health Outcome(s):** 

Ocular/Sensory; Mortality; Skin/Connective Tissue; Musculoskeletal; Thyroid;

Reported Health Effect(s):

Ocular/Sensory: Ophthalmoscopic examination (included in 90-day study only), histopathology (Zymbal's gland); Mortality: Mortality; Skin/Connective

Tissue: Histopathology (skin); Musculoskeletal: Histopathology (thigh muscle, sternebrae); Thyroid: Histopathology (thyroid);

**Duration:** Subchronic (>30-91 days) 90 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62965

Domain Domain 1: Test Substance	e Metric 1:	Metric	Rating	Comments
Domain 1: Test Substance		T. C.L.		
	Metric 1:	TD + C 1 + T1 + **		
		Test Substance Identity	High	All Outcomes: The test substance was identified definitively as "1,2-dichloroethane" and synonym "ethylene dichloride." The CASRN was listed as "100706-2" instead of 107-06-2, but this is assumed to be a typo.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from a commercial supplier.
	Metric 3:	Test Substance Purity	Medium	All Outcomes: It was noted that the purity of the test substance was verified by GCMS and no impurities were found; however, the numerical purity was not reported. Although the purity was not reported, this metric is rated as Medium because no impurities were found.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Corn oil vehicle controls were included.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: It was specified that animals were randomly allocated to vehicle and control groups.
Domain 3: Exposure Cha	racterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The test substance is volatile and was mixed fresh daily.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance administration appeared to be consistent across study groups and gavage volume was not excessive (0.1 mL/ 100g bw).
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were appropriate for the intended purpose of the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The rationale for the 90-day study was not specifically stated, but the 10-day study showed excessive mortality at the highest dose, 300 mg/kg/day, which was chosen because it was approximately 44% the LD50. The highest dose in the 90-day study was reduced in comparison (150 mg/kg/day).
	Metric 12:	Exposure Route and Method	High	All Outcomes: The oral route was appropriate for the test substance and study type.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Starting body weight was not reported, but the remaining characteristics were reported and appropriate. Animals were obtained from a commercial source.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: It was reported that animals were housed in a temperature- and humidity-controlled room, but the temperature and humidity were not reported. Remaining animal husbandry parameters were reported and appropriate.

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Study Citation: Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley

rats. Drug and Chemical Toxicology 17(4):463-477.

**Health Outcome(s):** 

Effect(s):

Ocular/Sensory; Mortality; Skin/Connective Tissue; Musculoskeletal; Thyroid;

**Reported Health** 

Ocular/Sensory: Ophthalmoscopic examination (included in 90-day study only), histopathology (Zymbal's gland); Mortality: Mortality; Skin/Connective

Tissue: Histopathology (skin); Musculoskeletal: Histopathology (thigh muscle, sternebrae); Thyroid: Histopathology (thyroid);

**Duration:** Subchronic (>30-91 days) 90 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	62965	, , , , , , , , , , , , , , , , , , , ,		
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: There were 10 animals/sex/group, which is considered appropriate for the 90-day study.
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Ocular/Sensory: The assessment methodologies (histopathology conducted by a veterinary pathologist and ophthalmoscopic examination) were reported and appropriate for the outcome of interest.; Mortality: The assessment methodology (daily cageside observation) was reported and appropriate for the outcome of interest.; Skin/Connective Tissue: The assessment methodology (histopathology conducted by a veterinary pathologist) was reported and appropriate for the outcome of interest.; Musculoskeletal: The assessment methodology (histopathology conducted by a veterinary pathologist) was reported and appropriate for the outcome of interest.; Thyroid: The assessment methodology (histopathology conducted by a veterinary pathologist) was reported and appropriate for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Ocular/Sensory: Outcome assessment appeared to be conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed for histopathology initially, which is standard practice.; Mortality: Outcome assessment was conducted consistently across control and treatment groups; "All rats were observed daily for physiological and behavioral responses as well as mortality."; Skin/Connective Tissue: Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially, which is standard practice.; Musculoskeletal: Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially, which is standard practice.; Thyroid: Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially, which is standard practice.
	Metric 18:	Sampling Adequacy	High	Ocular/Sensory: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Mortality: All rats were assessed for mortality; therefore, the sampling is adequate.; Skin/Connective Tissue: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Musculoskeletal: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.; Thyroid: All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.

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Study Citation:	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477.						
Health	Ocular/Sensory; Mortality; Skin/Connective Tissue; Musculoskeletal; Thyroid;						
Outcome(s): Reported Health	Ocular/Sensory: Ophthalmoscopic examination (included in 90-day study only), histopathology (Zymbal's gland); Mortality: Mortality; Skin/Connectiv						
Effect(s):	Tissue: Histopathology (skin); Musculoskeletal: Histopathology (thigh muscle, sternebrae); Thyroid: Histopathology (thyroid);						
Duration:	Subchronic (>30-91 days) 90 days						
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	62965	culanc- Isomer. 1,2-Diemoroculane					
Domain		Metric	Rating	Comments			
	Metric 19:	Blinding of Assessors	N/A	Ocular/Sensory: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Mortality: No subjective measurements were assessed.; Skin/Connective Tissue: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Musculoskeletal: No subjective measurements were assessed. Blinding is not required for initial histopathology review.; Thyroid: No subjective measurements were assessed. Blinding is not required for initial histopathology review.			
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were adequate.			
Damain & Canfaundi	na / Variabla Car	atual					
Domain 6: Confoundi	Metric 21:	Confounding Variables in Test Design	High	All Outcomes: The study protocol was well-described and no potentially confounding			
	Wicuic 21.	and Procedures	High	factors were identified.			
	Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: No health outcomes unrelated to exposure were identified that could influence the assessment.			
	Metric 23:	Data Presentation and Analysis	N/A	Ocular/Sensory: Statistical analysis is not necessary because no ophthalmoscopic or histopathological findings were observed for ocular/sensory organ samples (negative data).; Mortality: Statistical analysis was not conducted on mortality data; however, no deaths were observed so statistical analysis is not required.; Skin/Connective Tissue: Statistical analysis is not necessary because no histopathological findings were observed for skin samples (negative data).; Musculoskeletal: Statistical analysis is not necessary because no histopathological findings were observed for musculoskeletal samples (negative data).; Thyroid: Statistical analysis is not necessary because no histopathological findings were observed for thyroid samples (negative data).			
	Metric 24:	Reporting of Data	High	Ocular/Sensory: Negative findings were reported qualitatively.; Mortality: Mortality incidence data was provided.; Skin/Connective Tissue: Negative findings were reported qualitatively.; Musculoskeletal: Negative findings were reported qualitatively.; Thyroid: Negative findings were reported qualitatively.			

Study Citation:	Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley
·	rats. Drug and Chemical Toxicology 17(4):463-477.
Health	Gastrointestinal
Outcome(s):	

Histopathology (esophagus, stomach, duodenum, jejunum, tongue, salivary gland, ileum, colon, cecum, rectum) **Reported Health** 

Effect(s):

**Duration:** Subchronic (>30-91 days) 90 days

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62965

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified definitively as "1,2-dichloroethane" and synonym "ethylene dichloride." The CASRN was listed as "100706-2" instead of 107-06-2, but this is assumed to be a typo.
Metric 2:	Test Substance Source	High	The test article, 1,2-dichloroethane (1,2-DCE; CAS No. 100706-2) was purchased from Aldrich Chemical Co., (Milwaukee, WI); Lot. No. 0605 ML for the 10-day study and Lot. No. 9402 PL for the 90-day
Metric 3:	Test Substance Purity	Medium	It was noted that the purity of the test substance was verified by GCMS and no impurities were found; however, the numerical purity was not reported. Although the purity was not reported, this metric is rated as Medium because no impurities were found.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Corn oil vehicle controls were included.
Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	It was specified that animals were randomly allocated to vehicle and control groups.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test	High	The test substance is volatile and was mixed fresh daily.
Metric 8:	Substance Consistency of Exposure	High	Test substance administration appeared to be consistent across study groups and gavage
wienie o.	Administration	mgn	volume was not excessive (0.1 mL/ 100g bw).
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for the intended purpose of the study.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups, dose spacing, and magnitude of doses were adequate for the study. The rationale for the 90-day study was not specifically stated, but the 10-day study showed excessive mortality at the highest dose, 300 mg/kg/day, which was chosen because it was approximately 44% the LD50. The highest dose in the 90-day study was reduced in comparison (150 mg/kg/day).
Metric 12:	Exposure Route and Method	High	The oral route was appropriate for the test substance and study type.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Medium	Starting body weight was not reported, but the remaining characteristics were reported and appropriate. Animals were obtained from a commercial source.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	It was reported that animals were housed in a temperature- and humidity-controlled room, but the temperature and humidity were not reported. Remaining animal husbandr parameters were reported and appropriate.

Study Citation: Daniel, F.B., Robinson, M., Olson, G.R., York, R.G., Condie, L.W. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug and Chemical Toxicology 17(4):463-477.

Health

Gastrointestinal

Outcome(s):

**Reported Health** 

Histopathology (esophagus, stomach, duodenum, jejunum, tongue, salivary gland, ileum, colon, cecum, rectum)

Effect(s): Duration:

Subchronic (>30-91 days) 90 days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62965

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	There were 10 animals/sex/group, which is considered appropriate for the 90-day study.
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	High	The assessment methodology (histopathology conducted by a veterinary pathologist) was reported and appropriate for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment appeared to conducted consistently across control and treatment groups. A protocol is provided. Only the highest dose group was assessed initially, which is standard practice.
	Metric 18:	Sampling Adequacy	High	All 10 animals/sex/group were assessed for each endpoint; therefore, the sampling is adequate.
	Metric 19:	Blinding of Assessors	N/A	No subjective measurements were assessed. Blinding is not required for initial histopathology review.
	Metric 20:	Negative Control Response	High	The negative control responses were adequate.
Domain 6: Confounding	g / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	The study protocol was well-described and no potentially confounding factors were identified.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	No health outcomes unrelated to exposure were identified that could influence the assessment.
	Metric 23:	Data Presentation and Analysis	N/A	No statistical analysis was conducted on the histopathology data and no incidence data is provided. However, study authors indicate clearly negative findings.
	Metric 24:	Reporting of Data	Medium	Data were not shown, but are indicated as being negative in the text. For gross and histopathological findings, study authors state "few gross lesions were noted at the terminal sacrifice and most had a single incidence. None of the changes present showed a dose-response relationship and none were considered to be of toxicological significance." Data were

# **Overall Quality Determination**

# High

Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.

HERO ID: 1772372 Table: 1 of 4

**Study Citation:** 

Health Nutritional/Metabolic Outcome(s): **Reported Health** Body weights, growth, food intake Effect(s): **Duration:** Subchronic (>30-91 days) 90-days Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1772372 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High The test substance was definitively identified as 1,2-dichloroethane. A CASRN was not Metric 2: Test Substance Source High The test substance was sourced from Merk, the form was specified (liquid). Metric 3: Test Substance Purity High The test substance purity was 99% Domain 2: Test Design Negative and Vehicle Controls Metric 4: High A concurrent olive oil vehicle control was included. Metric 5: Positive Controls N/A Positive controls are not necessary for the study type. Metric 6: Randomized Allocation of Animals Low The study did not report the method of animal allocation, or whether other methods of normalization were used. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low The mg quantities of the test material for each dose group was "dissolved in 10 mL of olive oil"; however the test material was reported to be a liquid. The frequency of the Substance preparations and storage conditions were not specified. This could have a significant impact on the study results. Metric 8: Consistency of Exposure Low Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights Administration ranged from 40-60g, in which case, this gavage volume would be excessive. Metric 9: Reporting of Doses/Concentrations Medium It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on the results. Metric 10: **Exposure Frequency and Duration** Medium Animals were dosed via gavage 5 days per week for a period of 90 days. This deviates from the current OECD TG 408 guideline which specifies dosing 7 days/week. The study authors did not specifically justify the 5-day/week dosing schedule. Metric 11: Number of Exposure Groups and High The study included three exposure groups and a control. The dose spacing was based on the results of a preliminary study. Dose/Concentration Spacing Metric 12: Exposure Route and Method High Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although in the introduction, the authors noted that feeding studies were recommended by FAO/WHO. Domain 4: Test Animals Metric 13: **Test Animal Characteristics** High SPF Wistar rats were used. The animal starting body weights, sex, source, and age were specified. The test species were appropriate for the outcomes of interest. Continued on next page ...

		contin	ued from p	revious page			
Study Citation: Health	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Nutritional/Metabolic						
Outcome(s): Reported Health	Body weight	ts, growth, food intake					
Effect(s): Duration:	Subahrania	(>30-91 days) 90-days					
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	1772372	2001101 1,2 2101101001111110					
Domain		Metric	Rating	Comments			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry details were limited to food and water availability and the number of animals per cage (2/cage). Other details (e.g., temperature, humidity, light cycle), were not reported. Insufficient information was provided to determine whether there was consistency across groups.			
	Metric 15:	Number of Animals per Group	Medium	The study used 10/sex/group, with additional animals (8 males/group) added for clinical chemistry determinations at 4 and 8 weeks. The number of animals is consistent with current OECD guidelines for a 90-day oral toxicity study (TG 408).			
Domain 5: Outcome A	Assessment						
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was clearly reported and was sensitive and appropriate for the outcome(s) of interest.			
	Metric 17:	Consistency of Outcome Assessment	High	Based on the information provided, the outcome assessment protocol was applied consistently across all groups.			
	Metric 18:	Sampling Adequacy	Medium	The sample sizes for the specified outcomes were not included in the results tables. It is inferred from the methods that all animals were sampled.			
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary or required for outcomes that are either not subjective in nature, or are simple measures. Blinding is not recommended for initial histopathological examinations.			
	Metric 20:	Negative Control Response	High	No concerns were raised regarding the reported control responses.			
Domain 6: Confoundi	ng / Variable Co	ntrol					
Domain o. Comound	Metric 21:	Confounding Variables in Test Design and Procedures	High	The study reported most information to determine confounding (e.g., body weights and food intake), and there were no differences across groups.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods in general were described and were appropriate for the datasets.			
	Metric 24:	Reporting of Data	Low	Data were reported as means without measures of variance or n/group			
Overall Qual	lity Detern	nination	High				

HERO ID: 1772372 Table: 2 of 4

**Study Citation:** 

Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.

Health

Mortality

**Outcome(s):** 

Reported Health

Mortality

Effect(s):

**Duration:** Subchronic (>30-91 days) 90-days

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772372

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	The test substance was definitively identified as 1,2-dichloroethane. A CASRN was not provided.
	Metric 2:	Test Substance Source	High	The test substance was sourced from Merk, the form was specified (liquid).
	Metric 3:	Test Substance Purity	High	The test substance purity was 99%
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	A concurrent olive oil vehicle control was included.
	Metric 5:	Positive Controls	N/A	Positive controls are not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report the method of animal allocation, or whether other methods of normalization were used.
Domain 3: Exposure Cha	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	The mg quantities of the test material for each dose group was "dissolved in 10 mL of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. This could have a significant impact on the study results.
	Metric 8:	Consistency of Exposure Administration	Low	Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights ranged from 40-60g, in which case, this gavage volume would be excessive.
	Metric 9:	Reporting of Doses/Concentrations	Medium	It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on the results.
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were dosed via gavage 5 days per week for a period of 90 days. This deviates from the current OECD TG 408 guideline which specifies dosing 7 days/week. The study authors did not specifically justify the 5-day/week dosing schedule.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included three exposure groups and a control. The dose spacing was based on the results of a preliminary study.
	Metric 12:	Exposure Route and Method	High	Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.
Domain 4: Test Animals				
Domain 7. Test Amiliais	Metric 13:	Test Animal Characteristics	High	SPF Wistar rats were used. The animal starting body weights, sex, source, and age were specified. The test species were appropriate for the outcomes of interest.
		Cont	tinued on next page	•••

**Study Citation:** Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Mortality

Health

**Outcome(s):** 

Reported Health

Effect(s):

Mortality

**Duration:** Subchronic (>30-91 days) 90-days

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772372

Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry details were limited to food and water availability and the number of animals per cage (2/cage). Other details (e.g., temperature, humidity, light cycle), were not reported. Insufficient information was provided to determine whether there was consistency across groups.
	Metric 15:	Number of Animals per Group	Medium	The study used 10/sex/group, with additional animals (8 males/group) added for clinical chemistry determinations at 4 and 8 weeks. The number of animals is consistent with current OECD guidelines for a 90-day oral toxicity study (TG 408).
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	The study methods did not explicitly specify that animals were observed for mortality; however, mortality results were reported for the range-finding study so it was only assumed that mortality was also recorded for the 90-day study.
	Metric 17:	Consistency of Outcome Assessment	Low	No methods or details of animal observation for this outcome were provided. There is insufficient information for assessing consistency.
	Metric 18:	Sampling Adequacy	Medium	Details of sampling were not reported. However, it is assumed that all animals would be monitored for this outcome.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary or required for outcomes that are either not subjective in nature, or are simple measures. Blinding is not recommended for initial histopathological examinations.
	Metric 20:	Negative Control Response	Low	Control responses were not reported. Based on organ weight data, it does not appear as though any control males died (e.g., all were included in the endpoint assessment). However, only 9/10 control females were used for the same endpoint. It is unclear if this is an indication of animal death or the exclusion of an animal for other reasons.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	The study reported most information to determine confounding (e.g., body weights and food intake), and there were no differences across groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical methods in general were described. It is unclear whether statistical analysis was appropriate for this outcome because no results were reported.
	Metric 24:	Reporting of Data	Uninformative	No results for this outcome were reported.

# **Overall Quality Determination**

# Uninformative

**Study Citation:** 

Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.

HERO ID: 1772372 Table: 3 of 4

Health

Gastrointestinal; Musculoskeletal; Lung/Respiratory;

**Outcome(s):** 

**Reported Health** Gastrointestinal: Histopathology (stomach, salivary glands, intestines); Musculoskeletal: Histopathology (muscle); Lung/Respiratory: Histopathology

Effect(s): (lungs);

**Duration:** Subchronic (>30-91 days) 90-days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772372

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was definitively identified as 1,2-dichloroethane. A CASRN was not provided.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was sourced from Merk, the form was specified (liquid).
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance purity was 99%
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A concurrent olive oil vehicle control was included.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report the method of animal allocation, or whether other methods of normalization were used.
P : 4 E G				
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: The mg quantities of the test material for each dose group was "dissolved in 10 mL of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. This could have a significant impact on the study results.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights ranged from 40-60g, in which case, this gavage volume would be excessive.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on the results.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Animals were dosed via gavage 5 days per week for a period of 90 days. This deviates from the current OECD TG 408 guideline which specifies dosing 7 days/week. The study authors did not specifically justify the 5-day/week dosing schedule.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study included three exposure groups and a control. The dose spacing was based on the results of a preliminary study.
	Metric 12:	Exposure Route and Method	High	All Outcomes: Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.

Domain 4: Test Animals

... continued from previous page Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. **Study Citation:** Health Gastrointestinal; Musculoskeletal; Lung/Respiratory; Outcome(s): Reported Health Gastrointestinal: Histopathology (stomach, salivary glands, intestines); Musculoskeletal: Histopathology (muscle); Lung/Respiratory: Histopathology Effect(s): **Duration:** Subchronic (>30-91 days) 90-days Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 1772372 Metric Rating Comments Domain Metric 13: Test Animal Characteristics High All Outcomes: SPF Wistar rats were used. The animal starting body weights, sex, source, and age were specified. The test species were appropriate for the outcomes of interest. Metric 14: Adequacy and Consistency of Animal Low All Outcomes: Animal husbandry details were limited to food and water availability and **Husbandry Conditions** the number of animals per cage (2/cage). Other details (e.g., temperature, humidity, light cycle), were not reported. Insufficient information was provided to determine whether there was consistency across groups. Metric 15: Number of Animals per Group Medium All Outcomes: The study used 10/sex/group, with additional animals (8 males/group) added for clinical chemistry determinations at 4 and 8 weeks. The number of animals is consistent with current OECD guidelines for a 90-day oral toxicity study (TG 408). Domain 5: Outcome Assessment Metric 16: Gastrointestinal: The outcome assessment methodology available in the report was lim-Outcome Assessment Methodology Medium ited. Histopathology was conducted at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). Only tissues from control and high-dose animals were included. The assessment methods were consistent with those generally included in this study type and are considered to be sensitive and appropriate for assessing the outcome of interest.; Musculoskeletal: The outcome assessment methodology available in the report was limited. Histopathology was conducted at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). Only tissues from control and high-dose animals were included. The assessment methods were consistent with those generally included in this study type and are considered to be sensitive and appropriate for assessing the outcome of interest.; Lung/Respiratory: The outcome assessment methodology available in the report was limited. Histopathology was conducted at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). Only tissues from control and high-dose animals were included. Lung organ weights are generally included in this study type; however, histopathology is considered to be sensitive and appropriate for assessing the outcome of interest. Metric 17: Consistency of Outcome Assessment Medium All Outcomes: The timing of the outcome assessments was clearly reported. Although the methodological details were limited, there is no evidence that groups were treated inconsistently. Metric 18: Sampling Adequacy Medium All Outcomes: The sample sizes were included in the results for each endpoint. It is unclear why, for example, organ weight data were missing for some animals (e.g., sample sizes for female organ weights were 9, 8, 10, and 9 for the control, low, mid, and highdose groups, respectively), yet no deaths were reported. Similarly, histopathological examinations for some organs had sample sizes that were smaller than the number of animals/group. No explanations were provided. However, the number of animals examined for all endpoints was sufficient for conducting statistical analysis.

## ... continued from previous page

Study Citation: Health Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.

Gastrointestinal; Musculoskeletal; Lung/Respiratory;

**Outcome(s):** 

**Reported Health** 

Gastrointestinal: Histopathology (stomach, salivary glands, intestines); Musculoskeletal: Histopathology (muscle); Lung/Respiratory: Histopathology

**Effect(s):** (lungs)

**Duration:** Subchronic (>30-91 days) 90-days

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772372

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary or required for outcomes that are either not subjective in nature, or are simple measures. Blinding is not recommended for initial histopathological examinations.
	Metric 20:	Negative Control Response	High	All Outcomes: No concerns were raised regarding the reported control responses.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: The study reported most information to determine confounding (e.g., body weights and food intake), and there were no differences across groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment. Some animals were missing from some endpoints (e.g., not all 10 animals were sampled), but the reason for this was not specified.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods in general were described and were appropriate for the datasets.
	Metric 24:	Reporting of Data	High	All Outcomes: The results were reported quantitatively and included measures of sever-

# **Overall Quality Determination**

# Medium

Study Citation: Health				177). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Γhyroid; Neurological/Behavioral; Endocrine (Endocrine);	
Outcome(s): Reported Health Effect(s):  Duration:	Renal/Kidney: Organ weight, histopathology (urinary bladder, kidney); Immune/Hematological: Organ weight (spleen, thymus), histochemistry, histopathology; Cardiovascular: Organ weight (heart), histopathology (heart, aorta); Hepatic/Liver: organ weights; clinical chemistry (serum SGPT and ALP activity: 90-day study), BSP retention (both durations); in the liver (SGPT activity [preliminary study only], GL-6-Pase, AH and APDM activity [90-day only] and triglyceride content [both durations]); histopathology.; Thyroid: Organ weight, histopathology; Neurological/Behavioral: Organ weight (brain), histopathology (spinal cord, peripheral nerves, brain); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology (adrenals, pituitary, pancreas); Subchronic (>30-91 days) 90-days				
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:	1772372				
Domain		Metric	Rating	Comments	
Domain 1: Test Substan	ce Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was definitively identified as 1,2-dichloroethane. A CASRN was not provided.	
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was sourced from Merk, the form was specified (liquid).	
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance purity was 99%	
Domain 2: Test Design					
	Metric 4: Metric 5:	Negative and Vehicle Controls Positive Controls	High N/A	All Outcomes: A concurrent olive oil vehicle control was included.  All Outcomes: Positive controls are not necessary for the study type.	
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Positive controls are not necessary for the study type.  All Outcomes: The study did not report the method of animal allocation, or whether other methods of normalization were used.	
D : 1 E C	, . ,.				
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: The mg quantities of the test material for each dose group was "dissolved in 10 mL of olive oil"; however the test material was reported to be a liquid. The frequency of the preparations and storage conditions were not specified. This could have a significant impact on the study results.	
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Based on the text provided, it suggests that all animals were consistently administered a 10mL gavage volume, although there is some ambiguity. The starting body weights ranged from 40-60g, in which case, this gavage volume would be excessive.	
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: It was not specified whether the reported doses were target or nominal. There is no indication that any analytical measurements were conducted, but this is unlikely to have a substantial impact on the results.	
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Animals were dosed via gavage 5 days per week for a period of 90 days. This deviates from the current OECD TG 408 guideline which specifies dosing 7 days/week. The study authors did not specifically justify the 5-day/week dosing schedule.	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study included three exposure groups and a control. The dose spacing was based on the results of a preliminary study.	
		Contin	ued on next pa	age	

Study Citation: Health Outcome(s):	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Renal/Kidney; Immune/Hematological; Cardiovascular; Hepatic/Liver; Thyroid; Neurological/Behavioral; Endocrine (Endocrine);					
Reported Health Effect(s):	histopatholo ALP activity [90-day only (brain), histo pituitary, par	Renal/Kidney: Organ weight, histopathology (urinary bladder, kidney); Immune/Hematological: Organ weight (spleen, thymus), histochemistry, histopathology; Cardiovascular: Organ weight (heart), histopathology (heart, aorta); Hepatic/Liver: organ weights; clinical chemistry (serum SGPT and ALP activity: 90-day study), BSP retention (both durations); in the liver (SGPT activity [preliminary study only], GL-6-Pase, AH and APDM activity [90-day only] and triglyceride content [both durations]); histopathology.; Thyroid: Organ weight, histopathology; Neurological/Behavioral: Organ weight (brain), histopathology (spinal cord, peripheral nerves, brain); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology (adrenals, pituitary, pancreas);				
Duration: Chemical: HERO ID:		(>30-91 days) 90-days bethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
	Metric 12:	Exposure Route and Method	High	All Outcomes: Animals were dosed via gavage. The dosing method was appropriate for the test chemical, although in the introduction, the authors noted that feeding studies were recommended by FAO/WHO.		
Domain 4: Test Anima	nls					
	Metric 13:	Test Animal Characteristics	High	All Outcomes: SPF Wistar rats were used. The animal starting body weights, sex, source, and age were specified. The test species were appropriate for the outcomes of interest.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry details were limited to food and water availability and the number of animals per cage (2/cage). Other details (e.g., temperature, humidity, light cycle), were not reported. Insufficient information was provided to determine whether there was consistency across groups.		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The study used 10/sex/group, with additional animals (8 males/group) added for clinical chemistry determinations at 4 and 8 weeks. The number of animals is consistent with current OECD guidelines for a 90-day oral toxicity study (TG 408).		
Domain 5: Outcome A	assessment	Contin	ued on next pa			

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**Study Citation:** Health Outcome(s):

Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.

Renal/Kidney; Immune/Hematological; Cardiovascular; Hepatic/Liver; Thyroid; Neurological/Behavioral; Endocrine (Endocrine);

Reported Health

Effect(s):

Renal/Kidney: Organ weight, histopathology (urinary bladder, kidney); Immune/Hematological: Organ weight (spleen, thymus), histochemistry, histopathology; Cardiovascular: Organ weight (heart), histopathology (heart, aorta); Hepatic/Liver: organ weights; clinical chemistry (serum SGPT and ALP activity: 90-day study), BSP retention (both durations); in the liver (SGPT activity [preliminary study only], GL-6-Pase, AH and APDM activity [90-day only] and triglyceride content [both durations]); histopathology.; Thyroid: Organ weight, histopathology; Neurological/Behavioral: Organ weight (brain), histopathology (spinal cord, peripheral nerves, brain); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology (adrenals,

pituitary, pancreas);

**Duration:** Subchronic (>30-91 days) 90-days

Metric 17:

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID: 1772372

Domain

Metric Rating Metric 16: Outcome Assessment Methodology Medium

Comments Renal/Kidney: The outcome assessment methodology available in the report was lim-

ited. Organ weights were measured at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). No urinalysis or serum chemistry was included. Organ weights and histopathology are considered to be sensitive methods for assessing the outcome of interest.; Immune/Hematological: The outcome assessment methodology available in the report was limited. Hematological endpoints and organ weights were measured at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). The assessment methods are considered to be sensitive and appropriate methods for assessing the outcome of interest.; Cardiovascular: The outcome assessment methodology available in the report was limited. Organ weights were measured at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). The assessment methods were consistent with those included in this study type and are considered to be sensitive and appropriate methods for assessing the outcome of interest.; Hepatic/Liver: The outcome assessment methodology available in the report was limited. Several other studies were referred to for methods of measuring serum enzymes, liver enzyme activities, and for the BSP retention test. These references were not reviewed for this evaluation as many of these are established, uncomplicated methods. No methods for histopathology were provided (e.g., tissue fixation methods etc). All of the methods were considered to be sensitive for the outcome of interest.; Thyroid: The outcome assessment methodology available in the report was limited. Organ weights were measured at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). The assessment methods were consistent with those included in this study type and are considered to be sensitive and appropriate methods for assessing the outcome of interest.; Neurological/Behavioral: The outcome assessment methodology available in the report was limited. Organ weights were measured at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). This study type typically includes daily observations for changes in animal behavior. This study did not include clinical signs or detailed clinical observations.; Endocrine (Endocrine): The outcome assessment methodology available in the report was limited. Organ weights were measured at the time of sacrifice. No methods for histopathology were provided (e.g., tissue fixation methods etc). The assessment methods were consistent with those included in this study type and are considered to be sensitive and appropriate methods for assessing the outcome of interest. All Outcomes: The timing of the outcome assessments was clearly reported. Although

the methodological details were limited, there is no evidence that groups were treated

Continued on next page ...

Consistency of Outcome Assessment

Medium

inconsistently.

HERO ID: 1772372 Table: 4 of 4

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Study Citation: Health Outcome(s):		<del>-</del>		777). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Thyroid; Neurological/Behavioral; Endocrine (Endocrine);
Duration: Chemical: HERO ID:	Renal/Kidney: Organ weight, histopathology (urinary bladder, kidney); Immune/Hematological: Organ weight (spleen, thymus), histoche histopathology; Cardiovascular: Organ weight (heart), histopathology (heart, aorta); Hepatic/Liver: organ weights; clinical chemistry (serum SG ALP activity: 90-day study), BSP retention (both durations); in the liver (SGPT activity [preliminary study only], GL-6-Pase, AH and APDM [90-day only] and triglyceride content [both durations]); histopathology.; Thyroid: Organ weight, histopathology; Neurological/Behavioral: Organ (brain), histopathology (spinal cord, peripheral nerves, brain); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology (activity, pancreas); Subchronic (>30-91 days) 90-days 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1772372			
Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	Medium	All Outcomes: The sample sizes were included in the results for each endpoint. It is unclear why, for example, organ weight data were missing for some animals (e.g., sample sizes for female organ weights were 9, 8, 10, and 9 for the control, low, mid, and highdose groups, respectively), yet no deaths were reported. Similarly, histopathological examinations for some organs had sample sizes that were smaller than the number of an imals/group. No explanations were provided. However, the number of animals examine for all endpoints was sufficient for conducting statistical analysis.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary or required for outcomes that are either not subjective in nature, or are simple measures. Blinding is not recommended for initial histopathological examinations.
	Metric 20:	Negative Control Response	High	All Outcomes: No concerns were raised regarding the reported control responses.
Domain 6: Confoundi				
	Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: The study reported most information to determine confounding (e.g., body weights and food intake), and there were no differences across groups.

no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment. Some animals were missing from some endpoints (e.g., not all 10 animals were sampled), but the reason for this was not specified.; Endocrine (Endocrine): There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment. Some animals were missing from some endpoints (e.g., not all 10 animals were

All Outcomes: Statistical methods in general were described and were appropriate for

All Outcomes: Continuous data were reported as means without measures of variance.

sampled), but the reason for this was not specified.

		com	ntinued from previ	ious page
Study Citation: Health Outcome(s):	Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats. Renal/Kidney; Immune/Hematological; Cardiovascular; Hepatic/Liver; Thyroid; Neurological/Behavioral; Endocrine (Endocrine);  Renal/Kidney: Organ weight, histopathology (urinary bladder, kidney); Immune/Hematological: Organ weight (spleen, thymus), histochemistry histopathology; Cardiovascular: Organ weight (heart), histopathology (heart, aorta); Hepatic/Liver: organ weights; clinical chemistry (serum SGPT and ALP activity: 90-day study), BSP retention (both durations); in the liver (SGPT activity [preliminary study only], GL-6-Pase, AH and APDM activity [90-day only] and triglyceride content [both durations]); histopathology.; Thyroid: Organ weight, histopathology; Neurological/Behavioral: Organ weigh (brain), histopathology (spinal cord, peripheral nerves, brain); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology (adrenals			
Reported Health Effect(s):				
Duration:	pituitary, pancreas); Subchronic (>30-91 days) 90-days			
Chemical: HERO ID:		ethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Renal/Kidney: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment. Some animals were missing from some endpoints (e.g., not all 10 animals were sampled), but the reason for this was not specified.; Immune/Hematological: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment. Some animals were missing from some endpoints (e.g., not all 10 animals were sampled), but the reason for this was not specified.; Cardiovascular: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment. Some animals were missing from some endpoints (e.g., not all 10 animals were sampled), but the reason for this was not specified.; Hepatic/Liver: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.; Thyroid: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome surrelated to exposure (e.g., infection) that could influence the outcomes unrelated to exposure (e.g., infection) that could influence the outcome surrelated to exposure (e.g., infection) that could influence the outcomes unrelated to exposure (e.g., infection) that could influence the outcomes unrelated to exposure (e.g., infection) that could influence the outcome animals were missing from some endpoints (e.g.,

	Histopathology results included measures of severity.

Data Presentation and Analysis

Reporting of Data

Metric 23:

Metric 24:

## Continued on next page ...

High

Low

the datasets.

1,1-Dichloroethane

### ... continued from previous page

**Study Citation:** Esch, van, G. J., Kroes, R., Logten, van, M. J., Tonkelaar, den, E. M. (1977). Ninety-day toxicity study with 1,2-dichloroethane (DCE) in rats.

Health Outcome(s):

Reported Health

Effect(s):

Renal/Kidney; Immune/Hematological; Cardiovascular; Hepatic/Liver; Thyroid; Neurological/Behavioral; Endocrine (Endocrine);

Renal/Kidney: Organ weight, histopathology (urinary bladder, kidney); Immune/Hematological: Organ weight (spleen, thymus), histochemistry, histopathology; Cardiovascular: Organ weight (heart), histopathology (heart, aorta); Hepatic/Liver: organ weights; clinical chemistry (serum SGPT and

ALP activity: 90-day study), BSP retention (both durations); in the liver (SGPT activity [preliminary study only], GL-6-Pase, AH and APDM activity [90-day only] and triglyceride content [both durations]); histopathology.; Thyroid: Organ weight, histopathology; Neurological/Behavioral: Organ weight (brain), histopathology (spinal cord, peripheral nerves, brain); Endocrine (Endocrine): Organ weight (adrenals and pituitary), histopathology (adrenals,

HERO ID: 1772372 Table: 4 of 4

pituitary, pancreas);

**Duration:** Subchronic (>30-91 days) 90-days

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772372

Domain Metric Rating Comments **Overall Quality Determination** Medium

Study Citation: Health Outcome(s): Reported Health Effect(s): Duration: Chemical: HERO ID:	Mortality; N  Mortality: N  (rabbits and Subchronic	futritional/Metabolic; Hepatic/Liver;	·	1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.  iver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,2-dichloroethane was > 99%.
Domain 2: Test Design	36.1.4	N. C. IVIII C. C.	TT: 1	
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	aracterization			
Domain 5. Exposure Cir	Metric 7:	Preparation and Storage of Test	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a
	Weate 7.	Substance	Wediani	steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration).
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

## ... continued from previous page

Study Citation:				1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.
Health Outcome(s):	Mortality; N	utritional/Metabolic; Hepatic/Liver;		
Reported Health Effect(s): Duration: Chemical: HERO ID:	Mortality: Mortality; Nutritional/Metabolic: Body weights; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and ca (rabbits and cats), liver weight, and liver histology; Subchronic (>30-91 days) Up to 6 weeks - cats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1937626			iver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.
Domain 5: Outcome Ass	essment			
	Metric 16:	Outcome Assessment Methodology	High	Mortality: Mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition).; Nutritional/Metabolic: According to the methods, body weights were repeatedly monitored during the experimental period.; Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed based on information presented in the methods: serum ALT and AST, liver weight, and liver histology.
	Metric 17:	Consistency of Outcome Assessment	Low	Mortality: The time points in which mortality was assessed were not specified.; Nutritional/Metabolic: The time points in which body weights were assessed were not specified.; Hepatic/Liver: The time points in which clinical chemistry parameters related to liver function were assessed were not specified. Liver weights and/or histopathology were evaluated after the end of the 6-week study period (presumably in treated rats and controls).
	Metric 18:	Sampling Adequacy	High	Mortality: Mortality was assessed in all animals.; Nutritional/Metabolic: Body weights were presumably assessed in all animals.; Hepatic/Liver: Liver endpoints were presumably assessed in all animals.
	Metric 19:	Blinding of Assessors	N/A	Mortality: Blinding is not necessary for this outcome.; Nutritional/Metabolic: Blinding is not necessary for this outcome.; Hepatic/Liver: Blinding is not necessary for these outcomes.
	Metric 20:	Negative Control Response	High	Mortality: The study indicated that all cats (presumably treated cats and controls) survived 30 exposures.; Nutritional/Metabolic: The body weights of control animals were not specified.; Hepatic/Liver: Live data for control animals were not reported.
Domain 6: Confounding	/ Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
_				

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Study Citation: Health Outcome(s):	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Mortality; Nutritional/Metabolic; Hepatic/Liver;				
Reported Health	Mortality: 1	Mortality; Nutritional/Metabolic: Body	weights; Hepatic/Liv	er: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test	
Effect(s):	(rabbits and cats), liver weight, and liver histology;				
<b>Duration:</b>	Subchronic (>30-91 days) Up to 6 weeks - cats				
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1937626				
Domain		Metric	Rating	Comments	
	Metric 23:	Data Presentation and Analysis	N/A	Mortality: Statistical analysis was not performed/not necessary (clearly negative results across groups).; Nutritional/Metabolic: Statistical analysis was not performed/not necessary.; Hepatic/Liver: Statistical analysis was not performed/not necessary (negative results across groups).	
	Metric 24:	Reporting of Data	Medium	Mortality: The study reported survival qualitatively in the text (negative results, which presumably applied to both treated cats and controls).; Nutritional/Metabolic: There were presumably no effects on body weights in cats based on information presented in the text, but this was not explicitly stated. The study indicated that cats showed no "clinical symptoms" (weight loss was reported for other species within the same study).; Hepatic/Liver: There were presumably no effects on liver endpoints in cats based on information presented in the text (although this was not explicitly stated).	
Overall Qua	lity Deterr	nination	Medium		

HERO ID: 1937626 Table: 2 of 11

Domain 4: Test Animals

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** Cardiovascular Health Outcome(s): Reported Health Heart histology (1,2-dichloroethane only) Effect(s): **Duration:** Subchronic (>30-91 days) Up to 6 weeks - cats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1937626 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High The test substance was identified definitively as 1,2-dichloroethane. Metric 2: Test Substance Source High The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method. Metric 3: High The purity of 1,2-dichloroethane was > 99%. Test Substance Purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control. Metric 5: Positive Controls N/A Positive controls were not required by study type. Metric 6: Randomized Allocation of Animals Low The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and Substance passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results. Metric 8: Consistency of Exposure Medium It appeared that exposures were applied consistently across groups; however, limited details were provided. Administration Metric 9: Reporting of Doses/Concentrations Medium The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration. Metric 10: **Exposure Frequency and Duration** High The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks). Metric 11: Number of Exposure Groups and Medium The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-Dose/Concentration Spacing DCA and 1,2-DCA (at the same concentration). Metric 12: Exposure Route and Method Medium The study stated that dynamic air chambers were used without indicating the number of air changes.

HERO ID: 1937626 Table: 2 of 11

		CO1	ntinued from previous p	age				
Study Citation: Health	Hofmann, H Cardiovascu		ion toxicity of 1,1- and 1,7	2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.				
Outcome(s):	Cardiovascu	Cardiovascurai						
Reported Health Effect(s):	Heart histolo	ogy (1,2-dichloroethane only)						
Effect(s): Duration:	Subchronic (	(>30-91 days) Up to 6 weeks - cats						
Chemical:		bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	1937626	retime Isomer. 1,2 Diemereemane						
Domain		Metric	Rating	Comments				
	Metric 13:	Test Animal Characteristics	Medium	The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).				
	Metric 15:	Number of Animals per Group	Low	The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.				
Domain 5: Outcome As	aaaamant							
Domain 5: Outcome As	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment addressed the outcome of interest. Heart histology was evalu				
			, and the second	The outcome assessment addressed the outcome of interest. Heart histology was evaluated.				
	Metric 17:	Consistency of Outcome Assessment	Medium	Histology was evaluated at the end of the 6-week study period (presumably for treated cats and controls).				
	Metric 18:	Sampling Adequacy	High	Heart endpoints were presumably assessed in all animals.				
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.				
	Metric 20:	Negative Control Response	High	Heart data for control animals were not reported.				
Domain 6: Confounding	g / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information or respiration rates).				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.				
	Metric 23:	Data Presentation and Analysis	Uninformative	For heart histology, no statistical analyses were performed and data were not provided enabling independent analyses.				
	Metric 24:	Reporting of Data	Uninformative	The study reported cardiac dilatation in treated cats; however, no quantitative data for treated cats or controls were provided. Data for males and females were not discussed separately.				

#### **Overall Quality Determination** Uninformative

1,1-Dichloroethane

**Study Citation:** Health

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

HERO ID: 1937626 Table: 3 of 11

Immune/Hematological

**Outcome(s):** 

**Reported Health** 

Blood counts - specific parameters not specified (rats, rabbits, and cats only)

Effect(s):

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - cats **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	The purity of 1,2-dichloroethane was $>$ 99%.
Domain 2: Test Desig	rn			
Domain 2. Test Desig	Metric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Characterization			
Domain 3. Exposure	Metric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Giver that the test substance was analytically verified in the inhalation chamber, any omission are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration).
	Metric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

contir	nued from previo	ous page		
Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Immune/Hematological				
manific managementary material and analysis of contractions	hhita and aata ar	1)		
Blood counts - specific parameters not specified (rats, rabbits, and cats only)				
0.01 days) Up to 6 weeks _ cots				
Subchronic (>30-91 days) Up to 6 weeks - cats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
ine- isomer. 1,2-Diemoroculane				
Metric	Rating	Comments		
est Animal Characteristics	Medium	The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.		
Adequacy and Consistency of Animal Justin Gustandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).		
lumber of Animals per Group	Low	The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.		
N-4 A	M- 1:			
Outcome Assessment Methodology	Medium	The following assessments of were performed based on information presented in the methods: blood counts (specific parameters not specified). Note: Owing to the limited results reported, it is not entirely clear that hematology evaluations were performed.		
Consistency of Outcome Assessment	Low	The time points in which hematology parameters were assessed were not specified.		
ampling Adequacy	High	Blood counts were presumably assessed in all animals.		
slinding of Assessors	N/A	Blinding is not necessary for this outcome.		
legative Control Response	High	Hematology data for control animals were not reported.		
I				
Confounding Variables in Test Design	Medium	Reported information did not identify differences among study groups with respect to		
nd Procedures	Wedium	confounding factors; however, limited information was provided (e.g., no information o respiration rates).		
lealth Outcomes Unrelated to	Medium	There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.		
Data Presentation and Analysis	N/A	Statistical analysis was not performed/not necessary (negative results across groups).		
deporting of Data	Medium	There were presumably no effects on hematology endpoints in cats based on information presented in the text, but this was not explicitly stated. The study indicated that rats showed no "clinical symptoms."		
Pata Repo	Presentation and Analysis	Presentation and Analysis N/A rting of Data Medium		

HERO ID: 1937626 Table: 4 of 11

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** Health Renal/Kidney Outcome(s): Reported Health BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal"). Effect(s): **Duration:** Subchronic (>30-91 days) Up to 6 weeks - cats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1937626 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High The test substance was identified definitively as 1,2-dichloroethane. Metric 2: Test Substance Source High The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method. Metric 3: High The purity of 1,2-dichloroethane was > 99%. Test Substance Purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control. Metric 5: Positive Controls N/A Positive controls were not required by study type. Metric 6: Randomized Allocation of Animals Low The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and Substance passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results. Metric 8: Consistency of Exposure Medium It appeared that exposures were applied consistently across groups; however, limited details were provided. Administration Metric 9: Reporting of Doses/Concentrations Medium The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration. Metric 10: **Exposure Frequency and Duration** High The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks). Metric 11: Number of Exposure Groups and Medium The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-Dose/Concentration Spacing DCA and 1,2-DCA (at the same concentration). Metric 12: Exposure Route and Method Medium The study stated that dynamic air chambers were used without indicating the number of air changes. Domain 4: Test Animals

HERO ID: 1937626 Table: 4 of 11

		com	tinued from previous	page				
Study Citation: Health		Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Renal/Kidney						
Outcome(s): Reported Health Effect(s): Duration: Chemical: HERO ID:	statement in Subchronic (	BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal"). Subchronic (>30-91 days) Up to 6 weeks - cats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1937626						
Domain		Metric	Rating	Comments				
	Metric 13:	Test Animal Characteristics	Medium	The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).				
	Metric 15:	Number of Animals per Group	Low	The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.				
Domain 5: Outcome	Assessment							
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment addressed the outcome of interest. The following assessments of renal toxicity were performed: BUN and serum creatinine, urinary status (parameters not specified), kidney weights, and kidney histology.				
	Metric 17:	Consistency of Outcome Assessment	Low	The time points in which clinical chemistry parameters related to kidney function were assessed were not specified. Kidney weights and/or histology were evaluated at the end of the 6-week study period (presumably for treated cats and controls).				
	Metric 18:	Sampling Adequacy	High	Kidney endpoints were presumably assessed in all animals.				
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for these outcomes.				
	Metric 20:	Negative Control Response	High	Kidney data for control animals were not reported.				
Domain 6: Confound	ing / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.				
	Metric 23:	Data Presentation and Analysis	Uninformative	Statistical analysis was not performed/not necessary for kidney weights or histology (negative results across groups). For clinical chemistry parameters (i.e., BUN), no statistical analyses were performed and data were not provided enabling independent analyses.				
	Metric 24:	Reporting of Data	Uninformative	There were presumably no effects on kidney weights or kidney histology in cats based on information presented in the text, but this was not explicitly stated. The study reported that there was "an increasing trend of serum urea levels;" however, no quantitative data for treated cats or controls were provided. Data for males and females were not discussed separately.				

HERO ID: 1937626 Table: 4 of 11

1,1-Dichloroethane

## ... continued from previous page

Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a

**Effect(s):** statement indicating that results were "always normal").

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - cats **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain Metric Rating Comments

Overall Quality Determination Uninformative

HERO ID: 1937626 Table: 5 of 11

Study Citation: Health	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney;  Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;			
Outcome(s): Reported Health Effect(s):				
Duration:		(>30-91 days) Up to 6 weeks - rats		
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1937626			
Domain	1737020	Metric	Rating	Comments
Domain 1: Test Substance	ce	Wette	Rating	Comments
Domain 1, 10st Sucstant	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,2-dichloroethane was > 99%.
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	oroctarization			
Domain 3. Exposure Cir	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; how- ever, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks).
		C	Continued on next page	

HERO ID: 1937626 Table: 5 of 11

# ... continued from previous page

Study Citation: Health		. T., Birnstiel, H., Jobst, P. (1971). On inhala matological; Immune/Hematological; Hepatic		1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.
Outcome(s): Reported Health Effect(s):  Duration: Chemical: HERO ID:	Immune/Her parameters r and cats), liv findings eval Subchronic	matological: Blood counts - specific parame not specified (rats, rabbits, and cats only); H	ters not specified (rats, 1 epatic/Liver: Activities of BUN and serum creating	rabbits, and cats only); Immune/Hematological: Blood counts - specific of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits nine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine alts were "always normal").;
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Immune/Hematological: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, all exposed animals died by week 2, limiting the usefulness of the study.; Immune/Hematological: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 3 of 4 exposed rabbits died by week 4, limiting the usefulness of the study.; Hepatic/Liver: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 3 of 4 exposed rabbits died by week 4, limiting the usefulness of the study.; Renal/Kidney: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 3 of 4 exposed rabbits died by week 4, limiting the usefulness of the study.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Immune/Hematological: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Immune/Hematological: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Hepatic/Liver: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Renal/Kidney: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
		C	ontinued on next page .	

Study Citation:

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Outcome(s):

**Reported Health Effect(s):** 

Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits

and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine

findings evaluated; results not reported (other than a statement indicating that results were "always normal").;

Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney;

**Duration:** Chemical:

Subchronic (>30-91 days) Up to 6 weeks - rats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	Immune/Hematological: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Immune/Hematological: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rabbits/sex, when at least 5/sex/group are typically recommended for subchronic studies).; Hepatic/Liver: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group are typically recommended for subchronic studies).; Renal/Kidney: The study used fewer animals per group than that recommended for studies of this type (i.e. there were 2 rabbits/sex, when at least 5/sex/group are typically recommended for subchronic studies).

Metric 16: Outcome Assessment Methodology

High

Immune/Hematological: The following assessments of were performed based on information presented in the methods: blood counts (specific parameters not specified). Note: Owing to early mortality of the rats in this study and the limited results reported, it is not entirely clear that hematology evaluations were performed in rats.; Immune/Hematological: The following assessments of were performed based on information presented in the methods: blood counts (specific parameters not specified). Note: Owing to the limited results reported, it is not entirely clear that hematology evaluations were performed in rabbits. The study referred to "clinical-chemical examinations" that were done in rabbits (including evaluations of liver and kidney effects without explicitly mentioning blood analyses).; Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed based on information presented in the methods: serum ALT and AST, bromsulphthalein test, liver weight, and liver histology.; Renal/Kidney: The outcome assessment addressed the outcome of interest. The following assessments of renal toxicity were performed based on information presented in the methods: BUN, serum creatinine, urinary status (parameters not specified), kidney weight, and kidney histology.

HERO ID: 1937626 Table: 5 of 11

HERO ID: 1937626 Table: 5 of 11

## ... continued from previous page

Study Citation:
Health
Outcome(s):
Reported Health
Effect(s):
Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.
Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney;

Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;

Duration:

Subchronic (>30-91 days) Up to 6 weeks - rats

Chemical: HERO ID:	1,1-Dichloro 1937626	bethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Low	Immune/Hematological: The time points at which hematology parameters were assessed were not reported.; Immune/Hematological: The time points at which hematology parameters were assessed were not reported.; Hepatic/Liver: The time points at which clinical pathology endpoints related to liver function were assessed were not reported. Liver weights and/or histopathology were evaluated at the time of dissection of the dead animals (3 of 4 exposed rabbits died by week 4 of the 6-week study period) or after completion of the 6-week study period (the surviving animal). Control animals were presumably assessed histologically after completion of the 6-week study period.; Renal/Kidney: The time points at which clinical pathology endpoints related to renal function were assessed were not reported. Kidney weights and/or histopathology were evaluated at the time of dissection of the dead animals (3 of 4 exposed rabbits died by week 4 of the 6-week study period) or after completion of the 6-week study period (the surviving animal). Control animals were presumably assessed histologically after completion of the 6-week study period.
	Metric 18:	Sampling Adequacy	High	Immune/Hematological: Hematology endpoints were presumably monitored in all animals.; Immune/Hematological: Hematology endpoints were presumably monitored in all animals.; Hepatic/Liver: Liver endpoints were presumably monitored in all animals.; Renal/Kidney: Renal endpoints were presumably monitored in all animals.
	Metric 19:	Blinding of Assessors	N/A	Immune/Hematological: Blinding is not necessary for this outcome.; Immune/Hematological: Blinding is not necessary for this outcome.; Hepatic/Liver: Blinding is not necessary for these outcomes.; Renal/Kidney: Blinding is not necessary for these outcomes.
	Metric 20:	Negative Control Response	Low	Immune/Hematological: Data for hematology endpoints in control animals were not provided.; Immune/Hematological: Data for hematology endpoints in control animals were not provided.; Hepatic/Liver: Data for liver endpoints in control animals were not provided.; Renal/Kidney: Data for renal endpoints in control animals were not provided.
Domain 6: Confounding	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
		Cont	inued on next page	e

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Health Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Outcome(s): Reported Health Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits Effect(s): and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; **Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 1937626 Domain Metric Rating Comments Data Presentation and Analysis N/A Immune/Hematological: Statistical analysis was not performed/not necessary (results Metric 23: were presumably negative across groups).; Immune/Hematological: Statistical analysis was not performed/not necessary (results were presumably negative across groups).; Hepatic/Liver: Statistical analysis was not performed/not necessary for liver endpoints (results were presumably negative across groups).; Renal/Kidney: Statistical analysis was not performed/not necessary for renal endpoints (results were presumably negative across groups). Metric 24: Reporting of Data Medium Immune/Hematological: There were presumably no effects on hematology endpoints in rats based on information presented in the text, but this was not explicitly stated. The study indicated that rats showed no "characteristic symptoms" other than dyspnea.; Immune/Hematological: There were presumably no effects on hematology endpoints in rabbits based on information presented in the text, but this was not explicitly stated. The study indicated that rabbits clinical-chemical examinations of rabbits showed no "pathological findings."; Hepatic/Liver: There were presumably no effects on clinical pathology endpoints related to liver function, liver weight, or liver histology in rabbits based on qualitative information presented in the text. The study indicated that clinicalchemical examinations of rabbits showed no pathological findings with regard to liver function. No histopathological liver findings were reported (not explicitly stated that there were no effects).; Renal/Kidney: There were presumably no effects on clinical pathology endpoints related to renal function, kidney weight, or kidney histology in rabbits based on qualitative information presented in the text. The study indicated that clinical-chemical examinations of rabbits showed no pathological findings with regard to kidney function. No histopathological kidney findings were reported (not explicitly stated that there were no effects).

# **Overall Quality Determination**

# Uninformative

Study Citation: Health	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;			
Outcome(s): Reported Health Effect(s):	BUN and se	erum creatinine (rats, rabbits, and cats); kidn	ney weights, and kidney	ein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: histology. Urine findings evaluated; results not reported (other than a histology (1,2-dichloroethane/rats only); Mortality: Mortality; Mortality:
Duration: Chemical: HERO ID:		(>30-91 days) Up to 6 weeks - rats bethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce		6	
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,2-dichloroethane was > 99%.
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.
Damain 2. Evragura Ch	omo otomicrotion			
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks).
		Co	ontinued on next page .	••

1,1-Dichloroethane

## ... continued from previous page

Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

**Duration:** 

Chemical:

Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;

**Outcome(s):** 

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a

statement indicating that results were "always normal").; Lung/Respiratory: Lung histology (1,2-dichloroethane/rats only); Mortality: Mortality: Mortality:

HERO ID: 1937626 Table: 6 of 11

Mortality;

Subchronic (>30-91 days) Up to 6 weeks - rats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Hepatic/Liver: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, all exposed animals died by week 2, limiting the usefulness of the study.; Renal/Kidney: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, all exposed animals died by week 2, limiting the usefulness of the study.; Lung/Respiratory: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, all exposed animals died by week 2, limiting the usefulness of the study.; Mortality: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 3 of 4 exposed rabbits died by week 4, limiting the usefulness of the study.; Mortality: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 9 of 10 exposed guinea pigs died by week 3 (after 4-14 exposures), limiting the usefulness of the study.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

1,1-Dichloroethane

## ... continued from previous page

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;

Health

**Outcome(s):** 

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney:

BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Lung/Respiratory: Lung histology (1,2-dichloroethane/rats only); Mortality: Mortality; Mortality:

HERO ID: 1937626 Table: 6 of 11

Mortality;

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HEDO ID

HERO ID:	1937626			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	Hepatic/Liver: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Renal/Kidney: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Lung/Respiratory: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Mortality: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were reported.; Mortality: The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	Hepatic/Liver: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Renal/Kidney: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Lung/Respiratory: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Mortality: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group would typically be recommended).; Mortality: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).

Domain 5: Outcome Assessment

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** Health Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;

**Outcome(s):** 

**Reported Health** Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Lung/Respiratory: Lung histology (1,2-dichloroethane/rats only); Mortality: Mortality; Mortality:

HERO ID: 1937626 Table: 6 of 11

Mortality;

Duration: Chemical: HERO ID:		(>30-91 days) Up to 6 weeks - rats bethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	High	Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed based on information presented in the methods: serum ALT and AST, liver weight, and liver histology. Note: Owing to early mortality of the rats in this study and the limited results reported, it is not entirely clear that clinical pathology evaluations were performed in rats.; Renal/Kidney: The outcome assessment addressed the outcome of interest. The following assessments of renal toxicity were performed based on information presented in the methods: BUN, serum creatinine, urinary status (parameters not specified), kidney weight, and kidney histology. Note: Owing to early mortality of the rats in this study and the limited result reported, it is not entirely clear that clinical pathology evaluations were performed in rats.; Lung/Respiratory: The outcome assessment addressed the outcome of interest. The following assessments were performed: clinical signs and lung histology.; Mortality: Mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition). Based on the mortality data provided, it was not clear how frequently mortality: Mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition). Based on the mortality data provided, it was not clear how frequently mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition). Based on the mortality data provided, it was not clear how frequently mortality was evaluated (e.g., the study stated that guinea pigs typically died after 4-14 exposures).
	Metric 17:	Consistency of Outcome Assessment	Low	Hepatic/Liver: The time points at which clinical pathology endpoints related to liver function were assessed were not reported. Liver weights and/or histopathology were evaluated at the time of dissection of the dead animals (all exposed rats died by week 2 of the 6-week study period). Control animals were presumably assessed histologically after completion of the 6-week study period.; Renal/Kidney: The time points at which clinical pathology endpoints related to renal function were assessed were not reported. Kidney weights and/or histopathology were evaluated at the time of dissection of the dead animals (all exposed rats died by week 2 of the 6-week study period). Control animals were presumably assessed histologically after completion of the 6-week study period; Lung/Respiratory: The time points at which clinical signs were assessed were not reported. Lung histopathology was evaluated at the time of dissection of the dead animals (all exposed rats died by week 2 of the 6-week study period). Control animals were presumably assessed histologically after completion of the 6-week study period.; Mortality: The time points in which mortality was assessed were not specified.; Mortal ity: The time points in which mortality was assessed were not specified.
	Metric 18:	Sampling Adequacy	High	Hepatic/Liver: Liver endpoints were presumably monitored in all animals.; Renal/Kidney: Renal endpoints were presumably monitored in all animals.; Lung/Respiratory: Lung endpoints were presumably monitored in all animals.; Mortality: Mortality was assessed in all animals.; Mortality: Mortality was assessed in all animals.

... continued from previous page Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** Health Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality; Outcome(s): Reported Health Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a Effect(s): statement indicating that results were "always normal").; Lung/Respiratory: Lung histology (1,2-dichloroethane/rats only); Mortality; Mortality; Mortality; Mortality: **Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 1937626 Metric Comments Domain Rating Metric 19: Blinding of Assessors N/A All Outcomes: Blinding is not necessary for these outcomes. Metric 20: Negative Control Response Low Hepatic/Liver: Data for liver endpoints in control animals were not provided.; Renal/Kidney: Data for renal endpoints in control animals were not provided.; Lung/Respiratory: Data for respiratory endpoints in control animals were not provided.; Mortality: Mortality data for control animals were not reported.; Mortality: Mortality data for control animals were not reported. Domain 6: Confounding / Variable Control Metric 21: Confounding Variables in Test Design Medium All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no and Procedures information on respiration rates). Metric 22:

Health Outcomes Unrelated to Medium Exposure

Data Presentation and Analysis Metric 23:

Uninformative

All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.

HERO ID: 1937626 Table: 6 of 11

Hepatic/Liver: Statistical analysis was not performed/not necessary for clinical pathology or liver weights (results were presumably negative across groups). For liver histology, no statistical analysis was performed and data were not provided enabling independent analysis.; Renal/Kidney: Statistical analysis was not performed/not necessary for clinical pathology or kidney weights (results were presumably negative across groups). For kidney histology, no statistical analysis was performed and data were not provided enabling independent analysis.; Lung/Respiratory: For lung histology, no statistical analysis was performed and data were not provided enabling independent analysis.; Mortality: Statistical analysis was not performed, and data enabling statistical analysis were not provided.; Mortality: Statistical analysis was not performed, and data enabling

statistical analysis were not provided.

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

**Duration:** 

Chemical:

Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;

Outcome(s):

Reported Health Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: Effect(s):

BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Lung/Respiratory: Lung histology (1,2-dichloroethane/rats only); Mortality: Mortality; Mortality:

HERO ID: 1937626 Table: 6 of 11

reported in a table (mortality per week of the study). Separate data were not provided for males and females. However, data were not reported for controls.; Mortality: Mortality data were reported in a table (mortality per week of the study). Separate data were not provided for males and females. However, data were not reported for controls.

Mortality;

Subchronic (>30-91 days) Up to 6 weeks - rats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	1937626			
Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Uninformative	Hepatic/Liver: There were presumably no effects on clinical pathology endpoints related to liver function in rats based on information presented in the text, but this was not explicitly stated. The study indicated that rats showed no "characteristic symptoms" other than dyspnea. Fatty degeneration and necrosis of the liver were reported in treated rats. The report does not indicate the incidence of these effects in treated rats relative to controls. Data for males and females were not discussed separately.; Renal/Kidney: There were presumably no effects on clinical pathology endpoints related to renal function in rats based on information presented in the text, but this was not explicitly stated. The study indicated that rats showed no "characteristic symptoms" other than dyspnea. Lipoid nephrosis was reported in treated rats. The report does not indicate the incidence of this effect in treated rats relative to controls. Data for males and females were not discussed separately.; Lung/Respiratory: Treated rats showed dyspnea (frequency/incidence not reported). Low-grade breath and hyperemia were reported in treated rats. The report does not indicate the incidence of these effects in treated rats relative to controls. Data for males and females were not discussed separately.; Mortality data were

# **Overall Quality Determination**

# Uninformative

HERO ID: 1937626 Table: 7 of 11

1.1-Dichloroethane	Human Health Hazard

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands); Health Outcome(s): Reported Health Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine: Adrenal glands histology (1,2-dichloroethane/rats and guinea pigs only); Cardiovascular: Heart histology (1,2-dichloroethane only); Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine (Adrenal glands): Adrenal glands Effect(s): histology (1,2-dichloroethane/rats and guinea pigs only); **Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1937626 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: The test substance was identified definitively as 1,2-dichloroethane. Metric 2: Test Substance Source High All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method. Metric 3: All Outcomes: The purity of 1,2-dichloroethane was > 99%. Test Substance Purity High Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control. Metric 5: Positive Controls N/A All Outcomes: Positive controls were not required by study type. Metric 6: Randomized Allocation of Animals Low All Outcomes: The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered Substance air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results. Metric 8: Consistency of Exposure Medium All Outcomes: It appeared that exposures were applied consistently across groups; how-Administration ever, limited details were provided. Reporting of Doses/Concentrations Metric 9: Medium All Outcomes: The study indicated that the repeated analytical determination of 1,2dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration. **Exposure Frequency and Duration** High Metric 10: All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks).

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands); Health

**Outcome(s):** 

Reported Health Effect(s):

**Study Citation:** 

Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine: Adrenal glands histology (1,2-dichloroethane/rats and guinea pigs only); Cardiovascular: Heart histology (1,2-dichloroethane only); Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine (Adrenal glands): Adrenal glands

HERO ID: 1937626 Table: 7 of 11

histology (1,2-dichloroethane/rats and guinea pigs only);

**Duration: Chemical:**  Subchronic (>30-91 days) Up to 6 weeks - rats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Cardiovascular: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, all exposed animals died by week 2, limiting the usefulness of the study.; Endocrine: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, all exposed animals died by week 2, limiting the usefulness of the study.; Cardiovascular: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 3 of 4 exposed rabbits died by week 4, limiting the usefulness of the study.; Cardiovascular: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 9 of 10 exposed guinea pigs died by week 3 (after 4-14 exposures), limiting the usefulness of the study.; Endocrine (Adrenal glands): The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 9 of 10 exposed guinea pigs died by week 3 (after 4-14 exposures), limiting the usefulness of the study.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

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Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

**Health** Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);

**Outcome(s):** 

Reported Health

Effect(s):

Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine: Adrenal glands histology (1,2-dichloroethane/rats and guinea pigs only); Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine (Adrenal glands): Adrenal glands

histology (1,2-dichloroethane/rats and guinea pigs only);

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	1937626	retitatie 150mer. 1,2 Diemorocenane			
Domain		Metric	Rating	Comments	
	Metric 13:	Test Animal Characteristics	Medium	Cardiovascular: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Endocrine: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Cardiovascular: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Endocrine (Adrenal glands): The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Endocrine (Adrenal glands): The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).	
	Metric 15:	Number of Animals per Group	Low	Cardiovascular: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Endocrine: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Cardiovascular: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group are typically recommended for subchronic studies).; Cardiovascular: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).; Endocrine (Adrenal glands): The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).	

Domain 5: Outcome Assessment

Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health Cardiovascular; Endocrine; Cardiovascular; Endocrine (Adrenal glands);

**Outcome(s):** 

Reported Health Effect(s):

Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine: Adrenal glands histology (1,2-dichloroethane/rats and guinea pigs only); Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine (Adrenal glands): Adrenal glands

histology (1,2-dichloroethane/rats and guinea pigs only);

Duration: Chemical: HERO ID: Subchronic (>30-91 days) Up to 6 weeks - rats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

1937626

HERO ID:	193/626			
Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	High	Cardiovascular: The outcome assessment addressed the outcome of interest. The following assessments were performed: heart histology.; Endocrine: The outcome assessment addressed the outcome of interest. The following assessments were performed: adrenal glands histology.; Cardiovascular: The outcome assessment addressed the outcome of interest. The following assessments were performed: heart histology.; Cardiovascular: The outcome assessment addressed the outcome of interest. Heart histology was evaluated.; Endocrine (Adrenal glands): The outcome assessment addressed the outcome of interest. adrenal glands histology was evaluated.
	Metric 17:	Consistency of Outcome Assessment	Medium	Cardiovascular: Histopathology was evaluated at the time of dissection of the dead animals (all exposed rats died by week 2 of the 6-week study period). Control animals were presumably assessed histologically after completion of the 6-week study period.; Endocrine: Adrenal glands histopathology was evaluated at the time of dissection of the dead animals (all exposed rats died by week 2 of the 6-week study period). Control animals were presumably assessed histologically after completion of the 6-week study period.; Cardiovascular: Histopathology was evaluated at the time of dissection of the dead animals (3 of 4 exposed rabbits died by week 4 of the 6-week study period) or at the completion of the 6-week study period (the surviving animal). Control animals were presumably assessed histologically after completion of the 6-week study period.; Cardiovascular: Heart histopathology were evaluated at the time of dissection of the dead animals (9 of 10 exposed guinea pigs died by week 3 of the 6-week study period) or after completion of the 6-week study period.; Endocrine (Adrenal glands): Adrenal glands histopathology were evaluated at the time of dissection of the dead animals (9 of 10 exposed guinea pigs died by week 3 of the 6-week study period) or after completion of the 6-week study period (the surviving animal). Control animals were presumably assessed histologically after completion of the 6-week study period) or after completion of the 6-week study period (the surviving animal). Control animals were presumably assessed histologically after completion of the 6-week study period) or after completion of the 6-week study period (the surviving animal). Control animals were presumably assessed histologically after completion of the 6-week study period) or after completion of the 6-week study period (the surviving animal). Control animals were presumably assessed histologically after completion of the 6-week study period)
	Metric 18:	Sampling Adequacy	High	Cardiovascular: Heart histology was presumably evaluated in all animals.; Endocrine: Adrenal glands endpoints were presumably monitored in all animals.; Cardiovascular: Heart histology was presumably evaluated in all animals.; Cardiovascular: Heart endpoints were presumably monitored in all animals.; Endocrine (Adrenal glands): Adrenal glands endpoints were presumably monitored in all animals.
	Metric 19:	Blinding of Assessors	N/A	Cardiovascular: Blinding is not necessary for this outcome.; Endocrine: Blinding is not necessary for these outcomes.; Cardiovascular: Blinding is not necessary for this outcome.; Cardiovascular: Blinding is not necessary for these outcomes.; Endocrine (Adrenal glands): Blinding is not necessary for these outcomes.

HERO ID: 1937626 Table: 7 of 11

guinea pigs. The report does not indicate the incidence of this effect in treated guinea pigs relative to controls. Data for males and females were not discussed separately.

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**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);

Health **Outcome(s):** 

Reported Health

Effect(s):

Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine: Adrenal glands histology (1,2-dichloroethane/rats and guinea pigs only); Cardiovas-

cular: Heart histology (1,2-dichloroethane only); Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine (Adrenal glands): Adrenal glands

histology (1,2-dichloroethane/rats and guinea pigs only);

**Duration:** Chemical: Subchronic (>30-91 days) Up to 6 weeks - rats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	1937626			
Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	Low	Cardiovascular: Data for heart histology in control animals were not provided.; Endocrine: Data for adrenal glands endpoints in control animals were not provided.; Cardiovascular: Data for heart histology in control animals were not provided.; Cardiovascular: Data for heart endpoints in control animals were not provided.; Endocrine (Adrenal glands): Data for adrenal glands endpoints in control animals were not provided.
Domain 6: Confoun	ding / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Uninformative	Cardiovascular: For heart histology, no statistical analysis was performed and data were not provided enabling independent analysis.; Endocrine: For adrenal glands histology, no statistical analysis was performed and data were not provided enabling independent analysis.; Cardiovascular: For heart histology, no statistical analysis was performed and data were not provided enabling independent analysis.; Cardiovascular: For heart histology, no statistical analysis was performed and data were not provided enabling independent analysis.; Endocrine (Adrenal glands): For adrenal glands histology, no statistical analysis was performed and data were not provided enabling independent analysis.
	Metric 24:	Reporting of Data	Uninformative	Cardiovascular: Fatty degeneration and necrosis of the myocardium were reported in treated rats. The report does not indicate the incidence of this effect in treated rats relative to controls. Data for males and females were not discussed separately.; Endocrine: Lipoid storage in the adrenal glands was reported in treated rats. The report does not indicate the incidence of this effect in treated rats relative to controls. Data for males and females were not discussed separately.; Cardiovascular: Cardiac dilatation was reported in treated rabbits. The report does not indicate the incidence of this effect in treated rats relative to controls. Data for males and females were not discussed separately.; Cardiovascular: Fatty degeneration and necrosis of the myocardium were reported in treated guinea pigs. The report does not indicate the incidence of these effects in treated guinea pigs relative to controls. Data for males and females were not discussed separately.; Endocrine (Adrenal glands): Lipoid storage in the adrenal glands was reported in treated

# **Overall Quality Determination**

# Uninformative

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 1937626 Table: 7 of 11

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Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** 

Health Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);

**Outcome(s):** 

**Reported Health** Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine: Adrenal glands histology (1,2-dichloroethane/rats and guinea pigs only); Cardiovas-Effect(s):

cular: Heart histology (1,2-dichloroethane only); Cardiovascular: Heart histology (1,2-dichloroethane only); Endocrine (Adrenal glands): Adrenal glands

histology (1,2-dichloroethane/rats and guinea pigs only);

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain Metric Rating Comments

HERO ID: 1937626 Table: 8 of 11

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Nutritional/Metabolic: Nutritional/Metabolic: Health Outcome(s): Reported Health Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Effect(s): **Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1937626 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: The test substance was identified definitively as 1,2-dichloroethane. Metric 2: Test Substance Source High All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method. Metric 3: High All Outcomes: The purity of 1,2-dichloroethane was > 99%. Test Substance Purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control. Metric 5: Positive Controls N/A All Outcomes: Positive controls were not required by study type. Metric 6: Randomized Allocation of Animals Low All Outcomes: The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium All Outcomes: The study indicated that the test substance (in liquid form) was fed to a Substance steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results. Consistency of Exposure Metric 8: Medium All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided. Administration Metric 9: Reporting of Doses/Concentrations Medium All Outcomes: The study indicated that the repeated analytical determination of 1,2dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration. Metric 10: **Exposure Frequency and Duration** High All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks). Metric 11: Number of Exposure Groups and Uninformative Nutritional/Metabolic: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen Dose/Concentration Spacing to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, all exposed animals died by week 2, limiting the usefulness of the study.; Nutritional/Metabolic: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 3 of 4 exposed rabbits died by week 4, limiting the usefulness of the study. Continued on next page ...

		···cont	inued from previou	s page	
Study Citation: Health Outcome(s):	lealth Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;				
Reported Health Effect(s):					
Duration:	Subchronic (>30-91 days) Up to 6 weeks - rats				
Chemical:		bethane- Isomer: 1,2-Dichloroethane			
HERO ID:	1937626	,			
Domain		Metric	Rating	Comments	
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.	
Domain 4: Test Animals	3				
	Metric 13:	Test Animal Characteristics	Medium	Nutritional/Metabolic: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Nutritional/Metabolic: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).	
	Metric 15:	Number of Animals per Group	Low	Nutritional/Metabolic: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Nutritional/Metabolic: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group are typically recommended for subchronic studies).	
Domain 5: Outcome Ass	sessment				
Domain 3. Gateome 745	Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: According to the methods, body weights were repeatedly monitored during the experimental period.	
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: The time points at which body weights were assessed were not reported.	
	Metric 18:	Sampling Adequacy	High	All Outcomes: Body weights were presumably monitored in all animals.	
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this outcome.	
	Metric 20:	Negative Control Response	Low	All Outcomes: Body weight data for control animals was not reported.	
Domain 6: Confounding	r / Variable Co	ntrol			
Domain o. Comounting	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).	
	Metric 22:	Health Outcomes Unrelated to	Medium	All Outcomes: There was no information to indicate that there were differences among	
		Exposure		groups with respect to outcomes unrelated to exposure.	

HERO ID: 1937626 Table: 8 of 11

1,1-Dichloroethane

## ... continued from previous page

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** 

Health Nutritional/Metabolic; Nutritional/Metabolic;

**Outcome(s):** 

Reported Health

Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;

Effect(s):

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Medium	Nutritional/Metabolic: There were presumably no effects on body weights in rats based on information presented in the text, but this was not explicitly stated. The study indicated that rats did not show "characteristic symptoms" other than dyspnea (weight loss was reported for other species within the same study).; Nutritional/Metabolic: There were presumably no effects on body weights in rabbits based on information presented in the text, but this was not explicitly stated. The study indicated that rabbits did not show "characteristic symptoms" other than dyspnea (weight loss was reported for other species within the same study).

# **Overall Quality Determination**

# Uninformative

HERO ID: 1937626 Table: 9 of 11

1,1-Dichloroethane

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights

Effect(s):

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - guinea pigs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Substan	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	The purity of 1,2-dichloroethane was > 99%.
Domain 2: Test Design	l			
	Metric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	haracterization			
Domain 3. Exposure C	Metric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 9 of 10 exposed guinea pigs died by week 3 (after 4-14 exposures), limiting the usefulness of the study.
	Metric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Nutritional/Metabolic

Health

**Outcome(s):** 

Reported Health

Effect(s):

Body weights

**Duration:** 

Subchronic (>30-91 days) Up to 6 weeks - guinea pigs

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Metr	ric 13:	Test Animal Characteristics	Medium	The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.
Metr	ric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
Metr	ric 15:	Number of Animals per Group	Low	The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).
Domain 5: Outcome Assessmen	nt			
Metr	ric 16:	Outcome Assessment Methodology	Low	According to the methods, body weights were repeatedly monitored during the experimental period.
Metr	ic 17:	Consistency of Outcome Assessment	Low	The time points at which body weights were assessed were not reported.
Metr	ic 18:	Sampling Adequacy	High	Body weights were presumably monitored in all animals.
Metr	ic 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
Metr	ric 20:	Negative Control Response	Low	Body weight data for control animals was not reported.
Domain 6: Confounding / Varia	able Cor	ntrol		
Metr	ric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
Metr	ric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
Metr	ric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed/not necessary (a 10% change in body weight relative to controls could be used to determine biological significance).
Metr	ric 24:	Reporting of Data	Uninformative	The study reported body weight loss in treated guinea pigs; the change in body weight relative to controls was not reported quantitatively or qualitatively. Data were not described separately for males and females.

# **Overall Quality Determination**

# Uninformative

Human Health Hazard Animal Toxicology Evaluation HERO ID: 1937626 Table: 10 of 11 1,1-Dichloroethane

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

**Outcome(s): Reported Health**  Mortality Mortality

Effect(s):

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - rats Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	The purity of 1,2-dichloroethane was > 99%.
Domain 2: Test Desig	gn			
·	Metric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 2. Evmanum	Characterization			
Domain 3: Exposure	Metric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, all exposed animals died by week 2, limiting the usefulness of the study.
	Metric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

HERO ID: 1937626 Table: 10 of 11

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		c	ontinued from previous pa	age		
Study Citation: Health	Hofmann, H Mortality	Iofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.  Mortality				
Outcome(s):						
Reported Health	Mortality					
Effect(s):						
Duration:		(>30-91 days) Up to 6 weeks - rats				
Chemical:	,	bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	1937626					
Domain		Metric	Rating	Comments		
	Metric 13:	Test Animal Characteristics	Medium	The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).		
	Metric 15:	Number of Animals per Group	Low	The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).		
D						
Domain 5: Outcome	Assessment Metric 16:	Outcome Assessment Methodology	Medium	Mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition). Based on the mortality data provided, it was not clear how frequently mortality was evaluated (e.g., the study stated that rats typically died after 1-5 exposures).		
	Metric 17:	Consistency of Outcome Assessment	Low	The time points at which mortality was assessed were not reported.		
	Metric 18:	Sampling Adequacy	High	Mortality was monitored in all animals.		
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.		
	Metric 20:	Negative Control Response	Low	Mortality data for control animals was not reported.		
Di- (. Cf1	: / 37:					
Domain 6: Confound	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on		
				respiration rates).		
	Metric 22:	Health Outcomes Unrelated to	Medium	There was no information to indicate that there were differences among groups with		
		Exposure	· · · ·	respect to outcomes unrelated to exposure.		
	Metric 23:	Data Presentation and Analysis	Uninformative	Statistical analysis was not performed, and data enabling statistical analysis were not provided.		
	Metric 24:	Reporting of Data	Uninformative	Mortality data were reported in a table (mortality per week of the study). Separate data were not provided for males and females. However, data were not reported for controls.		
Overall Qua	lity Deterr	nination	Uninformative			
S TOTALL Qual						

HERO ID: 1937626 Table: 11 of 11

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** Health Hepatic/Liver; Renal/Kidney; Outcome(s): Reported Health Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a Effect(s): statement indicating that results were "always normal").; Subchronic (>30-91 days) Up to 6 weeks - guinea pigs **Duration:** Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane HERO ID: 1937626 Rating Domain Metric Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: The test substance was identified definitively as 1,2-dichloroethane. Metric 2: Test Substance Source High All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method. Metric 3: Test Substance Purity High All Outcomes: The purity of 1,2-dichloroethane was > 99%. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control. Metric 5: Positive Controls N/A All Outcomes: Positive controls were not required by study type. Metric 6: Randomized Allocation of Animals Low All Outcomes: The study did not report how animals were allocated to study groups. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered Substance air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results. Metric 8: Consistency of Exposure Medium All Outcomes: It appeared that exposures were applied consistently across groups; how-Administration ever, limited details were provided. Reporting of Doses/Concentrations Metric 9: Medium All Outcomes: The study indicated that the repeated analytical determination of 1,2dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 500 ppm exposure was reported (490 ppm); the reported analytical concentration was within 10% of the target concentration. **Exposure Frequency and Duration** High Metric 10: All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for up to 6 weeks). Metric 11: Number of Exposure Groups and Uninformative All Outcomes: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). The concentration was chosen to compare the Dose/Concentration Spacing toxicity of 1,1-DCA and 1,2-DCA (at the same concentration); however, 9 of 10 exposed guinea pigs died by week 3 (after 4-14 exposures), limiting the usefulness of the study. All Outcomes: The study stated that dynamic air chambers were used without indicating Metric 12: Exposure Route and Method Medium the number of air changes. Domain 4: Test Animals Continued on next page ...

Study Citation: Health Outcome(s):	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Hepatic/Liver; Renal/Kidney;  Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;				
Reported Health Effect(s):					
Duration: Chemical: HERO ID:	Subchronic (	(>30-91 days) Up to 6 weeks - guinea pigs bethane- Isomer: 1,2-Dichloroethane			
Domain		Metric	Rating	Comments	
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).	
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).	
Domain 5: Outcome A	ssessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Hepatic/Liver: The outcome assessment partially addressed the outcome of interest. The following assessments of liver toxicity were performed based on information presented in the methods: liver weight, and liver histology. No clinical pathology examinations were performed.; Renal/Kidney: The outcome assessment partially addressed the outcome of interest. The following assessments of renal toxicity were performed based on information presented in the methods: kidney weight, and kidney histology. Clinical pathology examinations were not performed.	
	Metric 17:	Consistency of Outcome Assessment	Medium	Hepatic/Liver: Liver weight and histology were assessed in the dissection of dead animals (9 of 10 exposed guinea pigs) or at the end of the 6-week study period (the surviving exposed animal). Control animals were presumably evaluated at the end of the 6-week study period.; Renal/Kidney: Kidney weights and/or histopathology were evaluated at the time of dissection of the dead animals (9 of 10 exposed guinea pigs died by week 3 of the 6-week study period) or after completion of the 6-week study period (the surviving animal). Control animals were presumably assessed histologically after completion of the 6-week study period.	
	Metric 18:	Sampling Adequacy	High	Hepatic/Liver: Liver endpoints were presumably monitored in all animals.; Renal/Kidney: Renal endpoints were presumably monitored in all animals.	
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for these outcomes.	
	Metric 20:	Negative Control Response	Low	Hepatic/Liver: Data for liver endpoints in control animals were not provided.; Renal/Kidney: Data for renal endpoints in control animals were not provided.	
Domain 6: Confoundin	ng / Variable Co	ntrol			
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).	
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.	
		Cont	tinued on next page		

HERO ID: 1937626 Table: 11 of 11

## ... continued from previous page

Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Health Hepatic/Liver; Renal/Kidney;

Outcome(s):

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a

statement indicating that results were "always normal").;

**Duration:** Subchronic (>30-91 days) Up to 6 weeks - guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID: 1937626

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Uninformative	Hepatic/Liver: For liver histology, no statistical analysis was performed and data were not provided enabling independent analysis.; Renal/Kidney: For kidney histology, no statistical analysis was performed and data were not provided enabling independent analysis.
	Metric 24:	Reporting of Data	Uninformative	Hepatic/Liver: Fatty degeneration and necrosis of the liver were reported in treated guinea pigs. The report does not indicate the incidence of these effects in treated guinea pigs relative to controls. Data for males and females were not discussed separately.; Renal/Kidney: Lipoid nephrosis was reported in treated guinea pigs. The report does not indicate the incidence of this effect in treated guinea pigs relative to controls. Data for males and females were not discussed separately.

# **Overall Quality Determination**

# Uninformative

Study Citation:	IRFMN, (1987). Report on the clinical chemistry results after 18 months inhalatory exposure - ethylene dichloride.
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**Health** Hepatic/Liver; Renal/Kidney; Immune/Hematological;

Outcome(s): Reported Health

**Effect(s):** 

Hepatic/Liver: Serum glucose, bilirubin, total protein, GOT, LDH, GPT, ALP, albumin, gamma GT; Renal/Kidney: BUN, CPK, Na, K, Ca, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.; Immune/Hematological: Hematology, serum alpha 2, alpha 2, and

beta globulins, urinary mucus, epithelial cells and microorganisms, urinary leukocytes, erythrocytes; **Duration:** Subchronic (>30-91 days) 18 months

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447260

Domain		Metric	Rating	Comments
Domain 1: Test Substance	e			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test material was identified as ethylene dichloride (EDC); CASRN 107-06-2
	Metric 2:	Test Substance Source	Low	All Outcomes: The source was provided; a batch and/or lot number was not specified.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity was reported (99.82%) and impurities were listed. These included 1,1-ethylene dichloride (0.02%), CCL4 (0.02%), benzene (0.09%), trichloroethylene (0.02%), and perchloroethylene (0.03%)
Domain 2: Test Design				
_	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Negative controls were exposed to air only under the same experimental conditions.
	Metric 5:	Positive Controls	N/A	Hepatic/Liver: This type of study does not require it.; Renal/Kidney: Not necessary for the study type.; Immune/Hematological: Not necessary for the study type.
	Metric 6:	Randomized Allocation of Animals	Medium	Hepatic/Liver: Animals were randomly assigned to study groups, the method of randomization was not specified.; Renal/Kidney: Animals were randomly assigned to study groups, the method of randomization was not specified; Immune/Hematological: Animals were randomly assigned to study groups, the method of randomization was not specified.
Domain 3: Exposure Cha	racterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: There was no mention of the method and equipment used to generate the test substance.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported (see examples in header) and the missing information is likely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: The exposure doses/concentrations or amounts of test substance were reported but with substantial ambiguity about precision (e.g., only target concentrations. Concentrations were purportedly monitored using GC, but no analytical values were provided Additionally, the exposure concentration in the high-exposure group was lowered from 250 ppm to 150 ppm. Another HERO ID (5447364) mentioned that the change occurred after 12 weeks, however, this was not specified in the current report.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Animals were exposed 7 hrs/day, 5 days/week; 6 hrs/day is typical, but this is unlikely to have a substantial impact on results.

		continu	ed from previ	ious page	
Study Citation: Health Outcome(s): Reported Health Effect(s):  Duration: Chemical: HERO ID:	IRFMN, (1987). Report on the clinical chemistry results after 18 months inhalatory exposure - ethylene dichloride. Hepatic/Liver; Renal/Kidney; Immune/Hematological;  Hepatic/Liver: Serum glucose, bilirubin, total protein, GOT, LDH, GPT, ALP, albumin, gamma GT; Renal/Kidney: BUN, CPK, Na, K, Ca, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.; Immune/Hematological: Hematology, serum alpha 2, alpha 2, and beta globulins, urinary mucus, epithelial cells and microorganisms, urinary leukocytes, erythrocytes; Subchronic (>30-91 days) 18 months 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 5447260				
Domain		Metric	Rating	Comments	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The number of exposure groups was adequate. The highest exposure concentration had to be decreased a few weeks after the start of exposure due to acute toxicity.	
	Metric 12:	Exposure Route and Method	Low	Hepatic/Liver: Some details of the exposure methods were provided in HERO ID 094773. Animals were exposed whole-body in stainless steel/glass chambers with no more than 270 animals per chamber. No details on whether the chambers were static or dynamic were provided; Renal/Kidney: Some details of the exposure methods were provided in HERO ID 094773. Animals were exposed whole-body in stainless steel/glass chambers with no more than 270 animals per chamber. No details on whether the chambers were static or dynamic were provided; Immune/Hematological: Only very minimal if any details about the methods for inhalation exposure administration (as described above) were reported, resulting in significant uncertainty about the true exposure parameters.	
Domain 4: Test Animals					
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Animal species, strain, and sex were reported. Based on the information provided animals may have been from an in-house colony. The animal age was mentioned in other reports (e.g., HERO ID 5447356), which indicated animals were 3 months of age at the start of the study.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Hepatic/Liver: Some animal husbandry conditions were provided in HERO ID 094773 including food and water availability, cage details, and room temperature. Animals were housed ten per cage. Humidity and light cycle were not specified. No differences were noted across groups; Renal/Kidney: Some animal husbandry conditions were provided in HERO ID 094773 including food and water availability, cage details, and room temperature. Animals were housed ten per cage. Humidity and light cycle were not specified. No differences were noted across groups.; Immune/Hematological: Some animal husbandry conditions were provided in HERO ID 094773 including food and water availability, cage details, and room temperature. Animals were housed ten per cage. Humidity and light cycle were not specified. No differences were noted across groups.	

HERO ID: 5447260 Table: 1 of 1

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**Study Citation:** IRFMN, (1987). Report on the clinical chemistry results after 18 months inhalatory exposure - ethylene dichloride.

Health

Effect(s):

Hepatic/Liver; Renal/Kidney; Immune/Hematological; **Outcome(s):** 

Reported Health

Hepatic/Liver: Serum glucose, bilirubin, total protein, GOT, LDH, GPT, ALP, albumin, gamma GT; Renal/Kidney: BUN, CPK, Na, K, Ca, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.; Immune/Hematological: Hematology, serum alpha 2, alpha 2, and

beta globulins, urinary mucus, epithelial cells and microorganisms, urinary leukocytes, erythrocytes;

**Duration:** Subchronic (>30-91 days) 18 months

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447260

Domain	Metric	Rating	Comments
Metric 15:	Number of Animals per Group	Low	Hepatic/Liver: The number of animals per group was not explicitly reported. 8-10 animals/sex/group were sacrificed at 18 months. It is unclear if this was the number of animals exposed or just the number of animals sampled. If this was the number of animals treated per group, it is less than recommended for a chronic study; Renal/Kidney: The number of animals per group was not explicitly reported. 8-10 animals/sex/group were sacrificed at 18 months. It is unclear if this was the number of animals exposed or just the number of animals sampled. If this was the number of animals treated per group, it is less than recommended for a chronic study.; Immune/Hematological: The number of animals per group was not explicitly reported. 8-10 animals/sex/group were sacrificed at 18 months. It is unclear if this was the number of animals exposed or just the number of animals sampled. If this was the number of animals treated per group, it is less than recommended for a chronic study
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	Low	Hepatic/Liver: The outcome assessment methodology was clearly reported. This reference only reports interim clinical chemistry, hematology, and urinalysis results. These endpoints are not sensitive for determining organ-specific toxicity and typically would be grouped with organ weight data and histopathology; Renal/Kidney: The outcome assessment methodology was clearly reported. This reference only reports interim clinical chemistry, hematology, and urinalysis results. These endpoints are not sensitive for determining organ-specific toxicity and typically would be grouped with organ weight data and histopathology; Immune/Hematological: The outcome assessment methodology was clearly reported. This reference only reports interim clinical chemistry, hematology, and urinalysis results. These endpoints are not sensitive for determining organ-specific toxicity and typically would be grouped with organ weight data and histopathology.
Metric 17:	Consistency of Outcome Assessment	High	Hepatic/Liver: Details regarding the execution of the study protocol for outcome assessment were provided (see HERO 062618). Blood was collected at the 18-month terminal sacrifice; Renal/Kidney: Details regarding the execution of the study protocol for outcome assessment were provided (see HERO 062618). Blood was collected at the 18-month terminal sacrifice.; Immune/Hematological: Details regarding the execution of the study protocol for outcome assessment were provided (see HERO 062618). Blood was collected at the 18-month terminal sacrifice.
Metric 18:	Sampling Adequacy	High	All Outcomes: The number of animals sampled (5 - 8/sex) was adequate for statistical analysis of the dataset.
Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary
Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate

Domain 6: Confounding / Variable Control

Continued on next page ...

		···continu	icu ii oiii picvi	ous page			
Study Citation: Health Outcome(s):		IRFMN, (1987). Report on the clinical chemistry results after 18 months inhalatory exposure - ethylene dichloride. Hepatic/Liver; Renal/Kidney; Immune/Hematological;					
Reported Health Effect(s):  Duration: Chemical: HERO ID:	Hepatic/Liver: Serum glucose, bilirubin, total protein, GOT, LDH, GPT, ALP, albumin, gamma GT; Renal/Kidney: BUN, CPK, Na, K, Ca, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.; Immune/Hematological: Hematology, serum alpha 2, alpha 2, and beta globulins, urinary mucus, epithelial cells and microorganisms, urinary leukocytes, erythrocytes; Subchronic (>30-91 days) 18 months 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 5447260						
Domain		Metric	Rating	Comments			
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: The study did not report information to determine confounding (i.e, not body weights or food or water intake. Respiratory rates were not reported, and the test material is expected to be a respiratory irritant.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: Details regarding animal attrition and health outcomes unrelated to exposure (e.g., infection) were reported for each study group and there were no difference among groups that could influence the outcome assessment. Blood work was not suggestive of the presence of infection.			
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed, with some methods described. Sufficient data were provided to conduct an independent statistical analysis.			
	Metric 24:	Reporting of Data	High	All Outcomes: The data were adequately reported, including individual animal data and means with a measure of variance.			

# **Overall Quality Determination**

# Medium

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Lung/Respiratory

Outcome(s):

**Reported Health** Respiratory rate, necropsy findings

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

IILKO ID.	.020001			
Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	Low	The source was not identified.
	Metric 3:	Test Substance Purity	Low	Purity was not reported.
Domain 2: Test Desig	gn			
·	Metric 4:	Negative and Vehicle Controls	Low	2 control rabbits were indicated, but the conditions of the controls were not described.
	Metric 5:	Positive Controls	N/A	Not required for the study design.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Characterization			
•	Metric 7:	Preparation and Storage of Test	Low	There was no mention of the method and equipment used to generate the test substance
	Metric 8:	Substance Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and the missing information is likely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Low	Actual concentrations were reported for the lowest concentration only and the analytica method used for this group was not specified.
	Metric 10:	Exposure Frequency and Duration	Uninformative	6 hours/day, 5 days/eek for 10 or 12 weeks for the 1.99 mg/l exposure group. Frequenc and duration of exposure information was not reported for the 4.0 mg/l treatment group which was part of a separate experiment.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	2 exposure groups were described, but the animals were not exposed concurrently (described as separate experiments).
	Metric 12:	Exposure Route and Method	Low	Only very minimal if any details about the methods for inhalation exposure administration were reported, resulting in significant uncertainty about the true exposure parameters. No information was provided on the generation of the test substance, chamber design or air changes.
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Uninformative	Only 2 animals/group were used.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Clinical signs were reported for each animal in text.
		Con	ntinued on next page .	

Study Citation: Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health Lung/Respiratory

Outcome(s):

**Reported Health** 

Respiratory rate, necropsy findings

Effect(s): Duration:

Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain	Metric		Comments
Metric 1	7: Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were confusing, limited, or not reported, and these deficiencies are likely to have a substantial impact on results. The length of follow up time was not given.
Metric 1	8: Sampling Adequacy	High	It appears that all animals were evaluated for clinical signs.
Metric 1	9: Blinding of Assessors	Medium	Blinding was not reported but this was not likely to affect the assessment of mortality.
Metric 2	0: Negative Control Response	Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding / Variable	Control		
Metric 2	1: Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
Metric 2	and Procedures 2: Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 2	3: Data Presentation and Analysis	N/A	Statistical analysis was not possible (2 rabbit/group)
Metric 2	4: Reporting of Data	High	Data for clinical signs were reported in text for each animal.

## **Overall Quality Determination**

Human Health Hazard Animal Toxicology Evaluation 1,1-Dichloroethane HERO ID: 4528351 Table: 2 of 6

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Gastrointestinal

**Outcome(s):** 

Reported Health

Diarrhea, necropsy findings

Effect(s):

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

11210 121	.020001			
Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2: Test Substance Source		Low	The source was not identified.
	Metric 3:	Test Substance Purity	Low	Purity was not reported.
Domain 2: Test Design				
Č	Metric 4:	Negative and Vehicle Controls	Low	2 control rabbits were indicated, but the conditions of the controls were not described.
	Metric 5:	Positive Controls	N/A	Not required for the study design.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Cl	haracterization			
Domain of Emposure of	Metric 7:	Preparation and Storage of Test	Low	There was no mention of the method and equipment used to generate the test substance
	Mario	Substance	T	
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and the missing informa- tion is likely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Low	Actual concentrations were reported for the lowest concentration only and the analytica
	Weare 3.	reporting of Boses, Concentrations	2011	method used for this group was not specified.
	Metric 10:	Exposure Frequency and Duration	Uninformative	6 hours/day, 5 days/eek for 10 or 12 weeks for the 1.99 mg/l exposure group. Frequency and duration of exposure information was not reported for the 4.0 mg/l treatment group which was part of a separate experiment.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	2 exposure groups were described, but the animals were not exposed concurrently (described as separate experiments).
	Metric 12:	Exposure Route and Method	Low	Only very minimal if any details about the methods for inhalation exposure administration were reported, resulting in significant uncertainty about the true exposure parameters. No information was provided on the generation of the test substance, chamber design or air changes.
Domain 4: Test Animal	c			
Domain 4. Test Allilla	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
		Husbandry Conditions	20	
	Metric 15:	Number of Animals per Group	Uninformative	Only 2 animals/group were used.
Domain 5: Outcome As	ssessment			
2 chair 5. Outcome 11	Metric 16:	Outcome Assessment Methodology	High	Incidence of diarrhea was reported for each animal in text.
		Cox	ntinued on next page .	

HERO ID: 4528351 Table: 2 of 6

#### ... continued from previous page

Study Citation: Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health Gastrointestinal

Outcome(s):

Reported Health Dia

Effect(s):

Diarrhea, necropsy findings

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain	Metric		Rating	Comments
Metr	ric 17:	Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were confusing, limited, or not reported, and these deficiencies are likely to have a substantial impact on results. The length of follow up time was not given.
Metr	ric 18:	Sampling Adequacy	High	It appears that all animals were evaluated for clinical signs.
Metr	ic 19:	Blinding of Assessors	N/A	Blinding is not necessary for the outcome being assessed.
Metr	ric 20:	Negative Control Response	Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding / Varia		trol		
Metr	ric 21:	Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
Metr	ric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metr	ric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not possible (2 rabbit/group)
Metr	ric 24:	Reporting of Data	High	Findings were reported in text for each animal.

## **Overall Quality Determination**

HERO ID: 4528351 Table: 3 of 6

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Neurological/Behavioral

**Outcome(s):** 

Reported Health

Clinical signs

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	Low	The source was not identified.
	Metric 3:	Test Substance Purity	Low	Purity was not reported.
Domain 2: Test Design				
Č	Metric 4:	Negative and Vehicle Controls	Low	2 control rabbits were indicated, but the conditions of the controls were not described.
	Metric 5:	Positive Controls	N/A	Not required for the study design.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test	Low	There was no mention of the method and equipment used to generate the test substance.
	Metric 8:	Substance Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and the missing information is likely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Low	Actual concentrations were reported for the lowest concentration only and the analytical method used for this group was not specified.
	Metric 10:	Exposure Frequency and Duration	Uninformative	6 hours/day, 5 days/eek for 10 or 12 weeks for the 1.99 mg/l exposure group. Frequency and duration of exposure information was not reported for the 4.0 mg/l treatment group, which was part of a separate experiment.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	2 exposure groups were described, but the animals were not exposed concurrently (described as separate experiments).
	Metric 12:	Exposure Route and Method	Low	Only very minimal if any details about the methods for inhalation exposure administration were reported, resulting in significant uncertainty about the true exposure parameters. No information was provided on the generation of the test substance, chamber design or air changes.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Uninformative	Only 2 animals/group were used.
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	High	Clinical signs were reported for each animal in text.
	<u> </u>	Cor	ntinued on next page .	••

# Human Health Hazard Animal Toxicology Evaluation

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**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Neurological/Behavioral

**Outcome(s):** 

**Reported Health** 

Clinical signs

Effect(s):

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain	Metric		Comments
Metric	17: Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were confusing, limited, or not reported, and these deficiencies are likely to have a substantial impact on results. The length of follow up time was not given.
Metric	18: Sampling Adequacy	Medium	It appears that all animals were evaluated for clinical signs.
Metric	19: Blinding of Assessors	Medium	Blinding was not reported but this was not likely to affect the assessment of mortality.
Metric 2	20: Negative Control Response	Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding / Variabl	e Control		
Metric 2	21: Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
Metric 2	and Procedures Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 2	23: Data Presentation and Analysis	N/A	Statistical analysis was not possible (2 rabbit/group)
Metric 2	24: Reporting of Data	High	Data for clinical signs were reported in text for each animal.

## **Overall Quality Determination**

HERO ID: 4528351 Table: 4 of 6

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

1,1-Dichloroethane

Mortality

**Outcome(s):** 

Reported Health

Deaths

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Metric	Rating	Comments
Test Substance Identity	High	The test substance was identified by a common chemical name.
Test Substance Source	Low	The source was not identified.
Test Substance Purity	Low	Purity was not reported.
Negative and Vehicle Controls	Low	2 control rabbits were indicated, but the conditions of the controls were not described.
Positive Controls	N/A	Not required for the study design.
Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Preparation and Storage of Test	Low	There was no mention of the method and equipment used to generate the test substance.
Substance Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and the missing information is likely to have a substantial impact on results.
Reporting of Doses/Concentrations	Low	Actual concentrations were reported for the lowest concentration only and the analytica method used for this group was not specified.
Exposure Frequency and Duration	Uninformative	6 hours/day, 5 days/eek for 10 or 12 weeks for the 1.99 mg/l exposure group. Frequency and duration of exposure information was not reported for the 4.0 mg/l treatment group, which was part of a separate experiment.
Number of Exposure Groups and Dose/Concentration Spacing	Low	2 exposure groups were described, but the animals were not exposed concurrently (described as separate experiments).
Exposure Route and Method	Low	Only very minimal if any details about the methods for inhalation exposure administration were reported, resulting in significant uncertainty about the true exposure parameters. No information was provided on the generation of the test substance, chamber design or air changes.
Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
Number of Animals per Group	Uninformative	Only 2 animals/group were used.
Outcome Assessment Methodology	High	Death of animals was reported in text.
	Husbandry Conditions Number of Animals per Group  Outcome Assessment Methodology	Husbandry Conditions Number of Animals per Group Uninformative

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane. **Health** Mortality

**Outcome(s):** 

Reported Health Deaths

Effect(s): Duration:

Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain	Metric		Rating	Comments
Met	ric 17:	Consistency of Outcome Assessment	Medium	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were confusing, limited, or not reported, and these deficiencies are likely to have a substantial impact on results. The length of follow up time was not given.
Meta	ric 18:	Sampling Adequacy	High	All animals were monitored for mortality
Meta	ric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
Meta	ric 20:	Negative Control Response	Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding / Vari	iable Con	trol		
Meta	ric 21:	Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
Met	ric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Meta	ric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not possible (2 rabbit/group)
Meta	ric 24:	Reporting of Data	High	Mortality data was reported in text.

## **Overall Quality Determination**

HERO ID: 4528351 Table: 5 of 6

**Study Citation:** 

Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Immune/Hematological

**Outcome(s):** 

Reported Health

Hematology

Effect(s):

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by a common chemical name.
	Metric 2:	Test Substance Source	Low	The source was not identified.
	Metric 3:	Test Substance Purity	Low	Purity was not reported.
Domain 2: Test Design				
Č	Metric 4:	Negative and Vehicle Controls	Low	2 control rabbits were indicated, but the conditions of the controls were not described.
	Metric 5:	Positive Controls	N/A	Not required for the study design.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test	Low	There was no mention of the method and equipment used to generate the test substance.
	Metric 8:	Substance Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and the missing information is likely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Low	Actual concentrations were reported for the lowest concentration only and the analytical method used for this group was not specified.
	Metric 10:	Exposure Frequency and Duration	Uninformative	6 hours/day, 5 days/eek for 10 or 12 weeks for the 1.99 mg/l exposure group. Frequency and duration of exposure information was not reported for the 4.0 mg/l treatment group, which was part of a separate experiment.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	2 exposure groups were described, but the animals were not exposed concurrently (described as separate experiments).
	Metric 12:	Exposure Route and Method	Low	Only very minimal if any details about the methods for inhalation exposure administration were reported, resulting in significant uncertainty about the true exposure parameters. No information was provided on the generation of the test substance, chamber design or air changes.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Uninformative	Only 2 animals/group were used.
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	Low	Methods for hematology assessment were not reported.
	<u> </u>	Cor	ntinued on next page .	

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Immune/Hematological

**Outcome(s):** 

Reported Health

Effect(s):
Duration:

Hematology

Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain	Metric	Rating	Comments
Metri	2 17: Consistency of Outcome A	Assessment Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were confusing, limited, or not reported, and these deficiencies are likely to have a substantial impact on results. Details regarding the timing of hematology assessment were not reported.
Metri	: 18: Sampling Adequacy	Low	It was not clear whether if hematology analysis was performed for all exposed rabbits.
Metri	e 19: Blinding of Assessors	N/A	Blinding is not necessary for the outcome being assessed.
Metri	20: Negative Control Respons	se Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding / Varia	ole Control		
Metri	21: Confounding Variables in	n Test Design Low	Body weight change and food/water intake were not reported.
Metri	and Procedures Health Outcomes Unrelate Exposure	ed to Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metri	23: Data Presentation and Ana	alysis N/A	Statistical analysis was not possible (2 rabbit/group)
Metri	24: Reporting of Data	Uninformative	The report does not provide data for specific exposure groups.

## **Overall Quality Determination**

HERO ID: 4528351 Table: 6 of 6

**Study Citation:** Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Decreased body weight

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

etric	Rating	Comments
nce Identity	High	The test substance was identified by a common chemical name.
nce Source	Low	The source was not identified.
nce Purity	Low	Purity was not reported.
nd Vehicle Controls	Low	2 control rabbits were indicated, but the conditions of the controls were not described.
ontrols	N/A	Not required for the study design.
d Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
and Storage of Test	Low	There was no mention of the method and equipment used to generate the test substance.
y of Exposure	Low	Details of exposure administration are insufficiently reported and the missing informa-
tion of Doses/Concentrations	Low	tion is likely to have a substantial impact on results.  Actual concentrations were reported for the lowest concentration only and the analytica method used for this group was not specified.
requency and Duration	Uninformative	6 hours/day, 5 days/eek for 10 or 12 weeks for the 1.99 mg/l exposure group. Frequency and duration of exposure information was not reported for the 4.0 mg/l treatment group which was part of a separate experiment.
of Exposure Groups and entration Spacing	Low	2 exposure groups were described, but the animals were not exposed concurrently (described as separate experiments).
coute and Method	Low	Only very minimal if any details about the methods for inhalation exposure administration were reported, resulting in significant uncertainty about the true exposure parameters. No information was provided on the generation of the test substance, chamber design or air changes.
al Characteristics	Low	The source, strain, sex, age, and starting body weight were not reported.
and Consistency of Animal Conditions	Low	Husbandry conditions were not reported.
Animals per Group	Uninformative	Only 2 animals/group were used.
ssessment Methodology	Medium	Body weight gain was reported for each animal at the end of the treatment (mean body weights were not shown).
.88		sessment Methodology Medium  Continued on next page

Study Citation: Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.

Health Nutritional/Metabolic

Outcome(s):

Reported Health

Decreased body weight

Effect(s):

**Duration:** Subchronic (>30-91 days) Inhalation - 6h/day, 5 days/week, 12 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4528351

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were confusing, limited, or not reported, and these deficiencies are likely to have a substantial impact on results. Timing of body weight measurements was not clearly consistent across groups.
	Metric 18:	Sampling Adequacy	High	Body weight was measured in all control and low concentration animals.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for the outcome being assessed.
	Metric 20:	Negative Control Response	Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding	ng / Variable Con Metric 21:	ntrol Confounding Variables in Test Design	Low	Body weight change and food/water intake were not reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There is no information to support or dismiss the suggestion that there was differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not possible (2 rabbit/group)
	Metric 24:	Reporting of Data	Low	Body weight gain was reported in text for each animal. Terminal body weights were not given.

# **Overall Quality Determination**

Study Citation:	Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro ass	ays to detect
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initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Cancer/Carcinogenesis

Outcome(s):

**Reported Health** Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)

Effect(s):

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Design				
· ·	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	Medium	Phenobarbital was used as a positive control for the tumor promotion protocol.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure Ch	aracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	The exposure period (5 days/week for 7 weeks) appears sufficient for determination of tumor promotion potential based on the positive control response.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only a single dose level was used, but it was justified as the MTD.
	Metric 12:	Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
Domain 4: Test Animals	2			
Domain 1. Test / minus	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome As	sessment			
2 cmain 5. Gateome 716	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment was appropriate and sensitive for tumor promotion potential.
	Metric 17:	Consistency of Outcome Assessment	High	Timing of necropsy was consistent across groups.
		Sampling Adequacy	High	Sample size (n = 9-10) was adequate for assessment of tumor promotion potential.

		contin	ued from p	orevious page					
Study Citation:		Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.							
Health	Cancer/Carc	1 0							
Outcome(s):									
Reported Health	Increased inc	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)							
Effect(s):									
<b>Duration:</b>	Subchronic (>30-91 days) 7 Weeks (promotion protocol)								
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane								
HERO ID:	200479								
Domain		Metric	Rating	Comments					
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology review.					
	Metric 20:	Negative Control Response	High	The biological response (incidence of GGT-positive foci) of the negative control group appeared adequate.					
Domain 6: Confound	ing / Variable Co	ntrol							
	Metric 21:	Confounding Variables in Test Design and Procedures	High	There is no evidence of confounding variables in test design and procedures that would affect tumor promotion.					
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	A low amount of attrition (0-1/10 animals) occurred in this experiment. However, there was no information provided either to support or dismiss the suggestion that differences among groups in health outcomes unrelated to exposure could influence the outcome					

Low

High

assessment.

Statistical analysis was performed, but the methods were not described.

Incidence data, with standard errors, are reported for each group in Table 4.

<b>Overall Quality Determination</b>	High
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Reporting of Data

Data Presentation and Analysis

Metric 23:

Metric 24:

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Decreased body weight gain (1,1,2-TCE only)

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

пекотр:	200479			
Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
	Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
	Metric 5:	Positive Controls	N/A	A positive control is not required for the endpoint of body weight.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Domain 3: Exposure	Characterization			
1	Metric 7:	Preparation and Storage of Test Substance	Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
	Metric 8:	Consistency of Exposure Administration	Low	Gavage volume is not reported for treated animals.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	Animals received the test substance by gavage 5 days/week for 7 weeks, which is appropriate for determining subchronic effects.
	Metric 11:	Number of Exposure Groups and	Medium	Only a single dose level was used, but it was justified as the MTD.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	The exposure route (gavage) was appropriate for the test substance.
D : 4 T : 4 :	1			
Domain 4: Test Anim	Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group (10) was appropriate for the study type and outcome analysis.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was appropriate. Body weight and body weight gain were measured.
	Metric 17:	Consistency of Outcome Assessment	Low	The timing of body weight measurements was not reported.
	Metric 18:	Sampling Adequacy	Low	Sample size for body weight and body weight gain was not reported.
		Contin	ued on next pa	age

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Decreased body weight gain (1,1,2-TCE only)

Effect(s):

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200479

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	The outcome (body weight) is not subjective.
	Metric 20:	Negative Control Response	Low	The biological response (body weight) of the negative control group was not reported.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Food and water were provided ad libitum. There is no evidence of confounding variables in test design and procedures that would affect the endpoint of body weight.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	A low amount of attrition (0-1/10 animals) occurred in this experiment. However, there was no information provided either to support or dismiss the suggestion that differences among groups in health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	Low	Results were described only in the text. Numerical values (i.e., body weight, body weight gain) were not provided. The absence of effects on body weight is implied but not explicitly stated.

## **Overall Quality Determination**

#### Medium

HERO ID: 200479 Table: 3 of 3

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Hepatic/Liver

**Outcome(s):** 

Reported Health

Decreased absolute liver weight (1,1,2-TCE only)

Effect(s):

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Metric 1: Test Substance Identity Metric 2: Test Substance Source Metric 3: Test Substance Source Metric 3: Test Substance Purity Medium Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals Medium					
Metric 1: Test Substance Identity Metric 2: Test Substance Source Metric 3: Test Substance Source Metric 3: Test Substance Purity Medium Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals Medium	Domain		Metric	Rating	Comments
Metric 2: Test Substance Source Metric 3: Test Substance Purity  Medium  The source was reported as Aldrich, but a batch or lot number was not provided.  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Medium  Medium  Medium  The study reports randomization of animals.  Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  The surve was reported as Aldrich, but a batch or lot number was not provided.  Medium  The surve was reported as 97 to 99%.  The study control is not required for the endpoint of liver weight.  Medium  The study does not report test substance storage and preparation conditions, and the to substance is volatile.  Gavage volume is not reported for treated animals.  Administration  Medium  Medium  Doses were reported without ambiguity in mg/kg.  Animals received the test substance by gavage 5 days/week for 7 weeks, which is appriate for determining subchronic effects.  Medium  Only a single dose level was used, but it was justified as the MTD.  Dose/Concentration Spacing  Metric 12: Exposure Route and Method  High  The exposure route (gavage) was appropriate for the test substance.	Domain 1: Test Substance	;			
Metric 3: Test Substance Purity  Medium Purity was reported as 97 to 99%.  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Medium The study reports randomization of animals.  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Metric 12: Exposure Route and Method  Metric 12: Exposure Force Reporting Spacing Metric 12: Exposure Route and Method  Metric 12: Exposure Force Reporting Spacing Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 12: Exposure Force Reposure Route and Method  Metric 12: Exposure Force Reposure Route and Method  Metric 12: Exposure Route and Method  Medium The study does not report test substance storage and preparation conditions, and the test substance is volatile.  Low Gavage volume is not reported for treated animals.  Metric 10: Gavage volume is not reported without ambiguity in mg/kg.  Metric 10: Exposure Frequency and Duration  High Doses were reported without ambiguity in mg/kg.  Metric 11: Number of Exposure Groups and Medium  Only a single dose level was used, but it was justified as the MTD.  Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 12: Exposure Foute (gavage) was appropriate for the test substance.	•	Metric 1:	Test Substance Identity	High	The test substance was identified by name.
main 2: Test Design  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Medium  The study reports randomization of animals.  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Wehicle Controls  High A concurrent negative control group received vehicle (corn oil) only.  Ad positive control is not required for the endpoint of liver weight.  Medium The study does not report test substance storage and preparation conditions, and the test substance is volatile.  Gavage volume is not reported for treated animals.  Administration Metric 9: Reporting of Doses/Concentrations High Doses were reported without ambiguity in mg/kg.  Metric 10: Exposure Frequency and Duration High Animals received the test substance by gavage 5 days/week for 7 weeks, which is apprinte for determining subchronic effects.  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method High The exposure route (gavage) was appropriate for the test substance.	•	Metric 2:	Test Substance Source	Low	The source was reported as Aldrich, but a batch or lot number was not provided.
Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Medium  Medium  The study reports randomization of animals.  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 13: A concurrent negative control group received vehicle (corn oil) only.  N/A A positive control is not required for the endpoint of liver weight.  Medium  The study does not report test substance storage and preparation conditions, and the to substance is volatile.  Gavage volume is not reported for treated animals.  Administration  Metric 19: Reporting of Doses/Concentrations High Doses were reported without ambiguity in mg/kg.  Animals received the test substance by gavage 5 days/week for 7 weeks, which is appriate for determining subchronic effects.  Medium Only a single dose level was used, but it was justified as the MTD.		Metric 3:	Test Substance Purity	Medium	Purity was reported as 97 to 99%.
Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Medium  Medium  The study reports randomization of animals.  Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  Metric 13: A concurrent negative control group received vehicle (corn oil) only.  N/A A positive control is not required for the endpoint of liver weight.  Medium  The study does not report test substance storage and preparation conditions, and the to substance is volatile.  Gavage volume is not reported for treated animals.  Administration  Metric 19: Reporting of Doses/Concentrations High Doses were reported without ambiguity in mg/kg.  Animals received the test substance by gavage 5 days/week for 7 weeks, which is appriate for determining subchronic effects.  Medium Only a single dose level was used, but it was justified as the MTD.	Domain 2: Test Design				
Metric 6: Randomized Allocation of Animals Medium The study reports randomization of animals.  Metric 7: Preparation and Storage of Test Low The study does not report test substance storage and preparation conditions, and the to substance is volatile.  Metric 8: Consistency of Exposure Low Gavage volume is not reported for treated animals.  Administration Metric 9: Reporting of Doses/Concentrations High Doses were reported without ambiguity in mg/kg.  Metric 10: Exposure Frequency and Duration High Animals received the test substance by gavage 5 days/week for 7 weeks, which is appriate for determining subchronic effects.  Metric 11: Number of Exposure Groups and Medium Only a single dose level was used, but it was justified as the MTD.  Dose/Concentration Spacing  Metric 12: Exposure Route and Method High The exposure route (gavage) was appropriate for the test substance.	_	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group received vehicle (corn oil) only.
main 3: Exposure Characterization  Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Low Gavage volume is not reported for treated animals.  Administration  Metric 9: Reporting of Doses/Concentrations High Doses were reported without ambiguity in mg/kg.  Metric 10: Exposure Frequency and Duration High Animals received the test substance by gavage 5 days/week for 7 weeks, which is appriate for determining subchronic effects.  Metric 11: Number of Exposure Groups and Doses/Concentration Spacing  Metric 12: Exposure Route and Method High The exposure route (gavage) was appropriate for the test substance.	-	Metric 5:	Positive Controls	N/A	A positive control is not required for the endpoint of liver weight.
Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration Metric 9: Exposure Frequency and Duration  Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  The study does not report test substance storage and preparation conditions, and the to substance is volatile.  Low Gavage volume is not reported for treated animals.  High Doses were reported without ambiguity in mg/kg.  Animals received the test substance by gavage 5 days/week for 7 weeks, which is appriate for determining subchronic effects.  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  High The exposure route (gavage) was appropriate for the test substance.		Metric 6:	Randomized Allocation of Animals	Medium	The study reports randomization of animals.
Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration Metric 9: Exposure Frequency and Duration  Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 12: Exposure Route and Method  The study does not report test substance storage and preparation conditions, and the to substance is volatile.  Low Gavage volume is not reported for treated animals.  High Doses were reported without ambiguity in mg/kg.  Animals received the test substance by gavage 5 days/week for 7 weeks, which is appriate for determining subchronic effects.  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  High The exposure route (gavage) was appropriate for the test substance.	Domain 3: Exposure Char	racterization			
Administration Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 13: Dose/Concentration Spacing  Metric 14: Metric 15: Exposure Route and Method  Metric 16: Dose/Concentration Spacing  Metric 17: Metric 18: Exposure Route and Method  Metric 19: Dose/Concentration Spacing  Metric 19: Dose/Concentration Spacing  Metric 10: Dose/Concentration Spacing	-			Low	The study does not report test substance storage and preparation conditions, and the test substance is volatile.
Metric 9: Reporting of Doses/Concentrations High Doses were reported without ambiguity in mg/kg.  Metric 10: Exposure Frequency and Duration High Animals received the test substance by gavage 5 days/week for 7 weeks, which is appriate for determining subchronic effects.  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method High The exposure route (gavage) was appropriate for the test substance.		Metric 8:		Low	Gavage volume is not reported for treated animals.
Metric 10: Exposure Frequency and Duration  High  Animals received the test substance by gavage 5 days/week for 7 weeks, which is app priate for determining subchronic effects.  Metric 11: Number of Exposure Groups and Medium  Dose/Concentration Spacing  Metric 12: Exposure Route and Method  High  Animals received the test substance by gavage 5 days/week for 7 weeks, which is app priate for determining subchronic effects.  Only a single dose level was used, but it was justified as the MTD.  Dose/Concentration Spacing  Metric 12: Exposure Route and Method  High  The exposure route (gavage) was appropriate for the test substance.		Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity in mg/kg.
Dose/Concentration Spacing Metric 12: Exposure Route and Method High The exposure route (gavage) was appropriate for the test substance.		Metric 10:		_	Animals received the test substance by gavage 5 days/week for 7 weeks, which is appropriate for determining subchronic effects.
Dose/Concentration Spacing Metric 12: Exposure Route and Method High The exposure route (gavage) was appropriate for the test substance.	-	Metric 11:	Number of Exposure Groups and	Medium	Only a single dose level was used, but it was justified as the MTD.
		Metric 12:		High	
and A. That Andread			•	<u>U</u>	1 6 67 11 1
nain 4: Test Animais	Domain 4: Test Animals				
Metric 13: Test Animal Characteristics Low Species, sex, strain, and starting body weight were reported. Age and source were not reported.		Metric 13:	Test Animal Characteristics	Low	Species, sex, strain, and starting body weight were reported. Age and source were not reported.
Metric 14: Adequacy and Consistency of Animal Low Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.	:	Metric 14:		Low	Temperature, humidity, and light-dark cycle were not reported and it is not possible to determine whether differences occurred between control and exposed populations.
Metric 15: Number of Animals per Group Medium The number of animals per study group (10) was appropriate for the study type and outcome analysis.	:	Metric 15:		Medium	
nain 5: Outcome Assessment	Domain 5: Outcome Asse	ssment			
Metric 16: Outcome Assessment Methodology Low The outcome assessment for liver was very limited (liver weight only).			Outcome Assessment Methodology	Low	The outcome assessment for liver was very limited (liver weight only)
Metric 17: Consistency of Outcome Assessment High Timing of necropsy was consistent across groups.			••		
Metric 18: Sampling Adequacy Low Sample size for liver weight measurements was not reported.				_	
Metric 19: Blinding of Assessors N/A The outcome (liver weight) is not subjective.					
Continued on next page			Continu	ued on next pa	nge

HERO ID: 200479 Table: 3 of 3

#### ... continued from previous page

Study Citation: Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., Tyson, C.A. (1988). Rat liver foci and in vitro assays to detect

initiating and promoting effects of chlorinated ethanes and ethylenes. Annals of the New York Academy of Sciences 534:521-530.

Health Hepatic/Liver

**Outcome(s):** 

**Reported Health** Decreased absolute liver weight (1,1,2-TCE only)

Effect(s):

**Duration:** Subchronic (>30-91 days) 7 Weeks (promotion protocol)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200479

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	Low	The biological response (liver weight) of the negative control group was not reported.
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	High	Food and water were provided ad libitum. There is no evidence of confounding variables in test design and procedures that would affect the endpoint of liver weight.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	A low amount of attrition (0-1/10 animals) occurred in this experiment. However, there was no information provided either to support or dismiss the suggestion that differences among groups in health outcomes unrelated to exposure could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed, but the methods were not described.
	Metric 24:	Reporting of Data	Low	Results were described only in the text. Numerical values (i.e., absolute and relative liver weights) were not provided. The absence of effects on liver weights is implied but not explicitly stated.

#### **Overall Quality Determination**

#### Medium

HERO ID: 62637 Table: 1 of 2

I _ I `	nch.	loroethane

Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health **Study Citation:** Perspectives 43:41-52. Immune/Hematological Health Outcome(s): Reported Health spleen and thymus weight, hematology, humoral immunity (spleen cell ab response), cell mediated immunity (delayed type hypersensitivity), spleen cell Effect(s): response to mitogens, function of reticuloendothelial system, gross necropsy **Duration:** Subchronic (>30-91 days) 90 day 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical: HERO ID: 62637 Domain Metric Comments Rating Domain 1: Test Substance Metric 1: Test Substance Identity High test substance identified by nomenclature Metric 2: Test Substance Source High test substance was obtained from commercial source and lot # provided Test Substance Purity Metric 3: Low Not reported Domain 2: Test Design Negative and Vehicle Controls Metric 4: High vehicle control Metric 5: Positive Controls Medium dexamethasone as a positive control for immune suppression Metric 6: Randomized Allocation of Animals Low animal allocation was not reported Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium preparation and storage conditions were incompletely reported but reported details indicate the authors attempted to mitigate test substance loss when bottles were changed out Substance every 3-4 days Metric 8: Consistency of Exposure Medium exposures were administered consistently across groups however water consumption was reduced in treated groups Administration Metric 9: Reporting of Doses/Concentrations High Doses were reported without ambiguity as calculated from consumption. **Exposure Frequency and Duration** Metric 10: High administration was appropriate for the study Number of Exposure Groups and Metric 11: Low number of groups was 3 treatment and a control and was adequate. Spacing did not Dose/Concentration Spacing encompass effects perhaps due to decreased consumption Exposure Route and Method Metric 12: Medium route and method of exposure was not suited to the test substance but the authors took steps to mitigate the problem Domain 4: Test Animals Metric 13: Test Animal Characteristics Medium animal characteristics were reported except starting body weight, animals were obtained from a commercial source and are appropriate Adequacy and Consistency of Animal Metric 14: High animal husbandry conditions were reported and consistent **Husbandry Conditions** Metric 15: Number of Animals per Group Medium animal number was reported 16-24/group and was appropriate Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology High assessment methodology was appropriate for the outcome of interest Metric 17: Consistency of Outcome Assessment High outcome assessment was consistent across study groups

Continued on next page ...

**Study Citation:** Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health

> Perspectives 43:41-52. Immune/Hematological

Health **Outcome(s):** 

Reported Health

Effect(s):

spleen and thymus weight, hematology, humoral immunity (spleen cell ab response), cell mediated immunity (delayed type hypersensitivity), spleen cell

HERO ID: 62637 Table: 1 of 2

response to mitogens, function of reticuloendothelial system, gross necropsy

Data Presentation and Analysis

Reporting of Data

Subchronic (>30-91 days) 90 day **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62637

Domain	Metric		Rating	Comments
	Metric 18:	Sampling Adequacy	High	sampling was adequate
	Metric 19:	Blinding of Assessors	N/A	Not necessary
	Metric 20:	Negative Control Response	High	negative controls responded appropriately
Domain 6: Confounding	ng / Variable Co	ntrol		
Bollium o. Comounum	Metric 21:	Confounding Variables in Test Design	Uninformative	decreased water consumption was reported in treated animals
	Metric 22:	and Procedures Health Outcomes Unrelated to	Medium	There was no information either to support or dismiss the suggestion that there were
		Exposure		differences among groups

## **Overall Quality Determination**

Metric 23:

Metric 24:

## Uninformative

High

High

methods were described and appropriate

data were reported for all groups negative data were reported in text

HERO ID: 62637 Table: 2 of 2

Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health **Study Citation:** Perspectives 43:41-52. Health Lung/Respiratory; Hepatic/Liver; Nutritional/Metabolic; Neurological/Behavioral; Renal/Kidney; Mortality; **Outcome(s):** Reported Health Lung/Respiratory: lung weight, gross necropsy; Hepatic/Liver: liver weight, gross necropsy; Nutritional/Metabolic: body weight, gross necropsy; Neuro-Effect(s): logical/Behavioral: brain weight, gross necropsy; Renal/Kidney: kidney weight, gross necropsy; Mortality: LD50; Subchronic (>30-91 days) 90 day **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 62637 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: test substance identified by nomenclature Metric 2: Test Substance Source High All Outcomes: test substance was obtained from commercial source and lot # provided Metric 3: **Test Substance Purity** Low All Outcomes: Not reported Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: vehicle control Positive Controls N/A Metric 5: All Outcomes: Not necessary for the study type Metric 6: Randomized Allocation of Animals Low All Outcomes: animal allocation was not reported Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium All Outcomes: preparation and storage conditions were incompletely reported but re-Substance ported details indicate the authors prepared the substance every 3-4 days and the amount lost was within 10% Metric 8: Consistency of Exposure Medium All Outcomes: exposures were administered consistently across groups however water Administration consumption was reduced in treated groups Metric 9: Reporting of Doses/Concentrations High Lung/Respiratory: doses were reported without ambiguity as calculated from consumption; Hepatic/Liver: doses were reported without ambiguity as calculated from consumption; Nutritional/Metabolic: Doses were reported without ambiguity as calculated from consumption.; Neurological/Behavioral: Doses were reported without ambiguity as calculated for consumption.; Renal/Kidney: doses were reported without ambiguity as calculated from consumption; Mortality: doses were reported without ambiguity as calculated from consumption Metric 10: **Exposure Frequency and Duration** High All Outcomes: administration was appropriate for the study Number of Exposure Groups and Metric 11: Low All Outcomes: number of groups was 3 treatment and a control and was adequate. Spacing did not encompass effects perhaps due to decreased consumption Dose/Concentration Spacing Metric 12: Exposure Route and Method Medium All Outcomes: route and method of exposure was not suited to the test substance but the authors took steps to mitigate the problem Domain 4: Test Animals Metric 13: Test Animal Characteristics Medium All Outcomes: animal characteristics were reported except starting body weight, animals were obtained from a commercial source and are appropriate Metric 14: Adequacy and Consistency of Animal High All Outcomes: animal husbandry conditions were reported and consistent **Husbandry Conditions** Metric 15: Number of Animals per Group Medium All Outcomes: animal number was reported 16-24/group and was appropriate Continued on next page ...

HERO ID: 62637 Table: 2 of 2

#### ... continued from previous page

Study Citation: Munson, A.E., Sanders, V.M., Douglas, K.A., Sain, L.E., Kauffmann, B.M., Jr., K.L. (1982). In vivo assessment of immunotoxicity. Environmental Health

Perspectives 43:41-52.

Health Lung/Respiratory; Hepatic/Liver; Nutritional/Metabolic; Neurological/Behavioral; Renal/Kidney; Mortality;

**Outcome(s):** 

Reported Health Lung/Respiratory: lung weight, gross necropsy; Hepatic/Liver: liver weight, gross necropsy; Nutritional/Metabolic: body weight, gross necropsy; Neuro-

Effect(s): logical/Behavioral: brain weight, gross necropsy; Renal/Kidney: kidney weight, gross necropsy; Mortality: LD50;

**Duration:** Subchronic (>30-91 days) 90 day

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62637

Domain		Metric	Rating	Comments
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: assessment methodology was appropriate for the outcome of interest but did not include histology
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: outcome assessment was consistent across study groups
	Metric 18:	Sampling Adequacy	High	All Outcomes: sampling was adequate
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary
	Metric 20:	Negative Control Response	High	All Outcomes: negative controls responded appropriately
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Uninformative	All Outcomes: decreased water consumption was reported in treated animals
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: methods were described and appropriate
	Metric 24:	Reporting of Data	High	All Outcomes: data were reported for all groups negative data were reported in text

## **Overall Quality Determination**

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

HERO ID: 5441108 Table: 1 of 4

**Study Citation:** 

Health		Nutritional/Metabolic					
Outcome(s):	1 (ddildolld)						
Reported Health	Bodyweight	, food consumption					
Effect(s):	J						
Duration:	Subchronic	(>30-91 days) 6-weeks-rats					
Chemical:	1,1-Dichloro	oethane- Isomer: 1,2-Dichloroethane					
HERO ID:	5441108						
Domain		Metric	Rating	Comments			
Domain 1: Test Substar	nce						
	Metric 1:	Test Substance Identity	High	The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN).			
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and the identity was not analytically verified by the performing laboratory.			
	Metric 3:	Test Substance Purity	Medium	Reported as technical grade; no additional information provided.			
Domain 2: Test Design	3.5	N. C. IVIII C. C.	TT: 1				
	Metric 4:	Negative and Vehicle Controls Positive Controls	High N/A	A negative corn-oil vehicle control group was included.			
	Metric 5: Metric 6:	Randomized Allocation of Animals	Low	Positive controls are not required for this study type.			
	Metric 6:	Randomized Anocation of Animais	Low	Allocation of test animals was not reported.			
Domain 3: Exposure Cl	naracterization						
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).			
	Metric 8:	Consistency of Exposure	Low	Gavage volumes not reported.			
	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	The doses were clearly reported; however, here is no indication that doses were analytically verified.			
	Metric 10:	Exposure Frequency and Duration	High	Animals were dosed 5 days per week for 6 weeks. Animals were observed for an additional 2-week recovery period. This was a preliminary study and the exposure frequency and duration were acceptable; however, the study was shorter in duration than a typical 90-day subchronic study, but longer than a 28-day study.			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 5 dose groups and a control. No justification for the doses and spacing were provided, but this was a range-finding/preliminary study. The dosing provided sufficient information to select doses for the chronic duration study.			
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.			
Domain 4: Test Animal							
	Metric 13:	Test Animal Characteristics	Medium	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. The Species, strain, ages, sex, and sources used for the chronic study were reported, and are assumed to be the same for the preliminary study but there is some uncertainty. Starting body weights were not provided.			
		Continu	ued on next pa	nge			
			Г.	<u> </u>			

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health Nutritional/Metabolic

Outcome(s):

**Reported Health** 

Bodyweight, food consumption

Effect(s):

**Duration:** Subchronic (>30-91 days) 6-weeks-rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal	Medium	Detailed animal husbandry conditions were provided for the chronic study and were
		Husbandry Conditions		adequate. It is presumed they were the same for the preliminary study, but this was not explicitly stated.
	Metric 15:	Number of Animals per Group	Medium	The study used 5 animals/sex/group. This is appropriate for a preliminary test.
Domain 5: Outcome A	ssessment			
Domain of Galcome 1	Metric 16:	Outcome Assessment Methodology	Medium	No details for the outcome assessment methodology (including the number and frequency of measurements) were provided. However, there are no concerns with sensitivity.
	Metric 17:	Consistency of Outcome Assessment	Low	The consistency of the outcome assessment cannot be determined with the information provided.
	Metric 18:	Sampling Adequacy	Low	Sampling details were not provided.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for this outcome
	Metric 20:	Negative Control Response	Low	The biological responses of the negative control group were not reported.
Domain 6: Confounding	ng / Variable Co	ntrol		
Domain o. Comounan	Metric 21:	Confounding Variables in Test Design	Low	The study did not report all information to determine confounding (e.g., initial body
	Medic 21.	and Procedures	2011	weights, food and water intake). Significant depressions in body weight were observed at higher doses, but this was considered to be a treatment-related response.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	The text is suggestive that statistical analysis was conducted; however, quantitative results were not provided in a manner that would allow for an independent analysis.
	Metric 24:	Reporting of Data	Low	Percent body weight depression was specified for some but not all dose groups. Although quantitative data (means $\pm$ measures of variance) were not provided, the qualitative statements were sufficient for determining the observed effects.

## **Overall Quality Determination**

## Medium

Study Citation: NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

Effect(s): Duration:

Subchronic (>30-91 days) 6-weeks-rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN).
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and the identity was not analytically verified by the performing laboratory.
	Metric 3:	Test Substance Purity	Medium	Reported as technical grade; no additional information provided.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	A negative corn-oil vehicle control group was included.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	Allocation of test animals was not reported.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure Administration	Low	Gavage volumes not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The doses were clearly reported; however, here is no indication that doses were analytically verified.
	Metric 10:	Exposure Frequency and Duration	High	Animals were dosed 5 days per week for 6 weeks. Animals were observed for an additional 2-week recovery period. This was a preliminary study and the exposure frequency and duration were acceptable; however, the study was shorter in duration than a typical 90-day subchronic study, but longer than a 28-day study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 5 dose groups and a control. No justification for the doses and spacing were provided, but this was a range-finding/preliminary study. The dosing provided sufficient information to select doses for the chronic duration study.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.
Domain 4: Test Animals	1			
	Metric 13:	Test Animal Characteristics	Medium	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. The Species, strain, ages, sex, and sources used for the chronic study were reported, and are assumed to be the same for the preliminary study but there is some uncertainty. Starting body weights were not provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Detailed animal husbandry conditions were provided for the chronic study and were adequate. It is presumed they were the same for the preliminary study, but this was not explicitly stated.

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

**Health** Mortality

**Outcome(s):** 

**Reported Health** Survival

Effect(s):

**Duration:** Subchronic (>30-91 days) 6-weeks-rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The study used 5 animals/sex/group. This is appropriate for a preliminary test.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	No details of the outcome assessment methodology were provided, but based on the text, it is evident that animals were observed for mortality until the end of the recovery period.
	Metric 17:	Consistency of Outcome Assessment	Medium	No information to assess the consistency of the outcome assessment were provided, except that rats were observed for the entire 8 weeks.
	Metric 18:	Sampling Adequacy	High	The available text suggests that all animals were observed for mortality, although results for some groups were not reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for this outcome (mortality)
	Metric 20:	Negative Control Response	Low	The biological responses of the negative control group were not reported.
Domain 6: Confound	ing / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report all information to determine confounding (e.g., initial body weights, food and water intake). Significant depressions in body weight were observed at higher doses, but this was considered to be a treatment-related response.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Uninformative	It is unclear whether the data were statistically analyzed and quantitative results were not provided in a manner that would allow for an independent analysis.
	Metric 24:	Reporting of Data	Low	Mortality for two dose groups were described in the text. No qualitative statement for the other groups was provided.

# **Overall Quality Determination**

Study Citation: NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Bodyweight, food consumption

Effect(s): Duration:

**Chemical:** 

Subchronic (>30-91 days) 6-weeks mice 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substanc	e			
	Metric 1:	Test Substance Identity	High	The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN).
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and the identity was not analytically verified by the performing laboratory.
	Metric 3:	Test Substance Purity	Medium	Reported as technical grade; no additional information provided.
Domain 2: Test Design				
S	Metric 4:	Negative and Vehicle Controls	High	A negative corn-oil vehicle control group was included.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	Allocation of test animals was not reported.
Domain 3: Exposure Cha	racterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could sub- stantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure Administration	Low	Gavage volumes not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The doses were clearly reported; however, here is no indication that doses were analytically verified.
	Metric 10:	Exposure Frequency and Duration	High	Animals were dosed 5 days per week for 6 weeks. Animals were observed for an additional 2-week recovery period. This was a preliminary study and the exposure frequency and duration were acceptable; however, the study was shorter in duration than a typical 90-day subchronic study, but longer than a 28-day study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 5 dose groups and a control. No justification for the doses and spacing were provided, but this was a range-finding/preliminary study. The dosing provided sufficient information to select doses for the chronic duration study.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. The Species, strain, ages, sex, and sources used for the chronic study were reported, and are assumed to be the same for the preliminary study but there is some uncertainty. Starting body weights were not provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Detailed animal husbandry conditions were provided for the chronic study and were adequate. It is presumed they were the same for the preliminary study, but this was not explicitly stated.

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Bodyweight, food consumption

Effect(s): **Duration:** 

**Chemical:** 

Subchronic (>30-91 days) 6-weeks mice 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The study used 5 animals/sex/group. This is appropriate for a preliminary test.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	No details for the outcome assessment methodology (including the number and frequency of measurements) were provided. However, there are no concerns with sensitivity.
	Metric 17:	Consistency of Outcome Assessment	Medium	No information to assess the consistency of the outcome assessment were provided, except that rats were observed for the entire 8 weeks.
	Metric 18:	Sampling Adequacy	Low	Sampling details were not provided.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for this outcome
	Metric 20:	Negative Control Response	Low	The biological responses of the negative control group were not reported.
Domain 6: Confoundi	ng / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report all information to determine confounding (e.g., initial body weights, food and water intake). Significant depressions in body weight were observed at higher doses, but this was considered to be a treatment-related response.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	The text is suggestive that statistical analysis was conducted; however, quantitative results were not provided in a manner that would allow for an independent analysis.
	Metric 24:	Reporting of Data	Low	Percent body weight depression was specified for some but not all dose groups. Although quantitative data (means $\pm$ measures of variance) were not provided, the qualitative statements were sufficient for determining the observed effects.

## **Overall Quality Determination**

## Medium

HERO ID: 5441108 Table: 4 of 4

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 6-weeks mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN).
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and the identity was not analytically verified by the performing laboratory.
	Metric 3:	Test Substance Purity	Medium	Reported as technical grade; no additional information provided.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	A negative corn-oil vehicle control group was included.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	Allocation of test animals was not reported.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure Administration	Low	Gavage volumes not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The doses were clearly reported; however, here is no indication that doses were analytically verified.
	Metric 10:	Exposure Frequency and Duration	High	Animals were dosed 5 days per week for 6 weeks. Animals were observed for an additional 2-week recovery period. This was a preliminary study and the exposure frequency and duration were acceptable; however, the study was shorter in duration than a typical 90-day subchronic study, but longer than a 28-day study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 5 dose groups and a control. No justification for the doses and spacing were provided, but this was a range-finding/preliminary study. The dosing provided sufficient information to select doses for the chronic duration study.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.
Domain 4: Test Animals	1			
	Metric 13:	Test Animal Characteristics	Medium	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. The Species, strain, ages, sex, and sources used for the chronic study were reported, and are assumed to be the same for the preliminary study but there is some uncertainty. Starting body weights were not provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Detailed animal husbandry conditions were provided for the chronic study and were adequate. It is presumed they were the same for the preliminary study, but this was not explicitly stated.

**Study Citation:** NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103. Mortality

Health

**Outcome(s):** 

Reported Health

Effect(s):

Survival

**Duration:** Subchronic (>30-91 days) 6-weeks mice **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The study used 5 animals/sex/group. This is appropriate for a preliminary test.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	No details for the outcome assessment methodology (including the number and frequency of measurements) were provided. However, there are no concerns with sensitivity.
	Metric 17:	Consistency of Outcome Assessment	Medium	No information to assess the consistency of the outcome assessment were provided, except that rats were observed for the entire 8 weeks.
	Metric 18:	Sampling Adequacy	Medium	The available text suggests that all animals were observed for mortality, although results for some groups were not reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for this outcome
	Metric 20:	Negative Control Response	Low	The biological responses of the negative control group were not reported.
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report all information to determine confounding (e.g., initial body weights, food and water intake). Significant depressions in body weight were observed at higher doses, but this was considered to be a treatment-related response.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Uninformative	No statistical analysis was specified and quantitative data (or results in controls) were not provided to allow for an independent analysis.
	Metric 24:	Reporting of Data	Low	Mortality data were described for some, but not all groups, including controls.

## **Overall Quality Determination**

<b>Study Citation:</b>	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice
	(drinking water and gavage studies).
Health	Hepatic/Liver
Outcome(s):	

Outcome(s):

**Reported Health** Organ weight; histopathology; serum chemistry

Effect(s):

**Duration:** Subchronic (>30-91 days) 13-week; gavage, F344 **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Use of vehicle (corn oil) control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure Cha	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; Dose formulations were stable for at least 3 weeks and were appropriately stored for no longer than this time. Samples were analyzed both immediately after mixing and after dosing showing no loss of chemical during dosing administration.
	Metric 8:	Consistency of Exposure	High	All groups were dosed with a 5mL/kg volume of the test solutions
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Target and analytical dose concentrations and the dose in mg/kg were clearly reported. Formulations were all within 10% of the target concentration, and there was no loss of chemical during dose administration
	Metric 10:	Exposure Frequency and Duration	High	5d/week for 13 weeks
	Metric 11:	Number of Exposure Groups and	High	6 dose-groups including controls
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex is appropriate for a rodent subchronic assay; 20 males were used for some groups to be used for hematology/clinical chemistry

		contin	ued from p	revious page
Study Citation: Health		ater and gavage studies).	hylene bichl	loride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice
Outcome(s): Reported Health Effect(s):	Organ weigh	nt; histopathology; serum chemistry		
Duration: Chemical: HERO ID:		(>30-91 days) 13-week; gavage, F344 pethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	Methodology for clinical chemistry and for tissue/organ-related weights and histology was clearly reported and sensitive for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol for organ weights and histology were reported and outcomes were assessed consistently across study groups that were being assessed (e.g., at the same time after initial exposure) using the same protocol for groups included in the assessment.
	Metric 18:	Sampling Adequacy	Low	Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females; Clinical chemistry and hematology was performed on males only, and only in the top 3 dose groups. Since all males in the highest group died, serum chemistry was only available for the 120 and 240 dose groups. The number of samples available at the collection timepoints varied, from 3 to 9 animals. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Medium	Negative control-related organ weights and serum chemistry/hematology parameters were appropriate; histopathology data were selectively reported and did not include all control response details for this target/organ system
Domain 6: Confoundir	ng / Variable Co	ntrol		
- Samuel	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding, although at week 9, one cage of female controls had decreased body weights and the study authors indicated this was possibly due to animals not receiving water.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Appropriate methods of statistical analyses of organ weights, serum chemistry, hematology, and histology data were used.
	Metric 24:	Reporting of Data	Low	Organ weight and relevant serum chemistry data were adequately presented.  Histopathology results for this tissue/organ system were not reported. The study appears to only report "select" histopathology results.
Overall Quali	ity Deterr	nination	High	

HERO ID: 1772371 Table: 2 of 26

Study Citation: Health	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mi (drinking water and gavage studies).  Mortality; Nutritional/Metabolic;  Mortality: Survival; Nutritional/Metabolic: Body weight, weight gain, water consumption;  Subchronic (>30-91 days) 13-week; gavage, F344 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1772371					
Outcome(s): Reported Health Effect(s):						
Duration: Chemical: HERO ID:						
Domain		Metric	Rating	Comments		
Domain 1: Test Substance		T ( S ) ( ) I ) ( )	TT' 1	Allo and a long that the long		
	Metric 1: Metric 2: Metric 3:	Test Substance Identity Test Substance Source Test Substance Purity	High High High	All Outcomes: Name, sturcture and CASRN provided All Outcomes: Commercial source, analytically verified All Outcomes: 99% purity		
D : 0 T : D :			-			
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Use of vehicle (corn oil) control		
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type		
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers		
Domain 3: Exposure Cha	aracterization					
Donam 3. Exposure Cir	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Details of preparation were provided. Chemical stability was evaluated; Dose formulations were stable for at least 3 weeks and were appropriately stored for no longer than this time. Samples were analyzed both immediately after mixing and after dosing showing no loss of chemical during dosing administration.		
	Metric 8:	Consistency of Exposure	High	All Outcomes: All groups were dosed with a 5mL/kg volume of the test solutions		
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Target and analytical dose concentrations and the dose in mg/kg were clearly reported. Formulations were all within 10% of the target concentration, and there was no loss of chemical during dose administration		
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: 5d/week for 13 weeks		
	Metric 11:	Number of Exposure Groups and	High	All Outcomes: 6 dose-groups including controls		
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance		
Domain 4. Tt A:- 1						
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 10/sex is appropriate for a rodent subchronic assay		
Domain 5: Outcome Ass	recement					
Domain 5: Outcome Ass	sessment	C. A.	nued on nex			

HERO ID: 1772371 Table: 2 of 26

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Study Citation: Health	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mic (drinking water and gavage studies).  Mortality; Nutritional/Metabolic;						
Outcome(s):							
Reported Health Effect(s):	Mortality: Survival; Nutritional/Metabolic: Body weight, weight gain, water consumption;						
Duration:	Subchronic (>30-91 days) 13-week; gavage, F344						
Chemical:	1.1-Dichloroethane- Isomer: 1.2-Dichloroethane						
HERO ID:	1772371						
Domain		Metric	Rating	Comments			
	Metric 16:	Outcome Assessment Methodology	High	Mortality: Animals were observed for mortality; Nutritional/Metabolic: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.			
	Metric 17:	Consistency of Outcome Assessment	High	Mortality: Animals from all groups were consistently observed for this endpoint.; Nutritional/Metabolic: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol in all study groups.			
	Metric 18:	Sampling Adequacy	High	Mortality: All animals were assessed for this endpoint; Nutritional/Metabolic: All animals were assessed for this endpoint; final body weight means and weight change were based on animals surviving until the end of the study.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.			
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).			
Domain 6: Confoundir	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding, although at week 9, one cage of female controls had decreased body weights and the study authors indicated this was possibly due to animals not receiving water.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was not performed for this outcome, but sufficient data as provided to conduct independent analysis.			
	Metric 24:	Reporting of Data	High	Mortality: Survival data were clearly reported for all groups including controls.; Nutritional/Metabolic: Growth curves, initial and final body weights, and weight change data were clearly reported.			
Overall Quali	ity Detern	nination	High				

HERO ID: 1772371 Table: 3 of 26

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Study Citation:	NTP, (1991)	. Toxicity studies of 1,2-dichloroethane (etl	hylene bichl	oride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice					
TT 1/1		ater and gavage studies).	•						
Health Outcome(s):	Cardiovascular; Reproductive/Developmental; Renal/Kidney;								
Reported Health	Cardiovascu	Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight (Testis); histopathology; Renal/Kidney: Organ weight;							
Effect(s):	histopatholo		cproductive	7Developmental. Organ weight (Testis), histopathology, Kehal/Kidney. Organ weight,					
Duration:		(>30-91 days) 13-week; gavage, F344							
Chemical:		pethane- Isomer: 1,2-Dichloroethane							
HERO ID:	1772371								
Domain		Metric	Rating	Comments					
Domain 1: Test Substan									
	Metric 1:	Test Substance Identity	High	All Outcomes: Name, sturcture and CASRN provided					
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source, analytically verified					
	Metric 3:	Test Substance Purity	High	All Outcomes: 99% purity					
Domain 2: Test Design									
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Use of vehicle (corn oil) control					
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type					
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers					
Domain 3: Exposure Ch		D	II: -1.						
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Details of preparation were provided. Chemical stability was evaluated; Dose formulations were stable for at least 3 weeks and were appropriately stored for no longer than this time. Samples were analyzed both immediately after mixing and after dosing showing no loss of chemical during dosing administration.					
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: All groups were dosed with a 5mL/kg volume of the test solutions					
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target and analytical dose concentrations and the dose in mg/kg were clearly reported. Formulations were all within 10% of the target concentration, and there was no loss of chemical during dose administration					
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: 5d/week for 13 weeks					
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: 6 dose-groups including controls					
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance					
Domain 4: Test Animals	3								
Domain 1. 1000 / Hillings	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.					
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.					
		Contin	nued on nex	ct page					

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<b>Study Citation:</b>	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice
	(drinking water and gavage studies).

Health

Cardiovascular; Reproductive/Developmental; Renal/Kidney;

Outcome(s): Reported Health

Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight (Testis); histopathology; Renal/Kidney: Organ weight;

**Effect(s):** histopathology;

**Duration:** Subchronic (>30-91 days) 13-week; gavage, F344 **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

HERO ID:	1//23/1			
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	Cardiovascular: 10/sex is appropriate for a rodent subchronic assay; Reproductive/Developmental: 10/sex is appropriate for a rodent subchronic assay; Renal/Kidney: 10/sex is appropriate for a rodent subchronic assay; 20 males were used for some groups to be used for hematology/clinical chemistry
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Cardiovascular: Methodology for tissue/organ-related weights and histology was clearly reported and sensitive for the outcome of interest.; Reproductive/Developmental: Methodology was clearly reported and sensitive for the outcome of interest.; Renal/Kidney: Methodology for clinical chemistry and for tissue/organ-related weights and histology was clearly reported and sensitive for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Cardiovascular: Details of the outcome assessment protocol for organ weights and histology were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol for groups included in the assessment.; Reproductive/Developmental: Details of the outcome assessment were reported and outcomes were assessed consistently across the study groups included in this endpoint; Renal/Kidney: Details of the outcome assessment protocol for organ weights and histology were reported and outcomes were assessed consistently across study groups that were being assessed (e.g., at the same time after initial exposure) using the same protocol for groups included in the assessment.
	Metric 18:	Sampling Adequacy	Low	Cardiovascular: Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.; Reproductive/Developmental: Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.; Renal/Kidney: Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females; Clinical chemistry and hematology was performed on males only, and only in the top 3 dose groups. Since all males in the highest group died, serum chemistry was only available for the 120 and 240 dose groups. The number of samples available at the collection timepoints varied, from 3 to 9 animals. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.

Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (Testis); histopathology; Renal/Kidney: Organ weight;
(Testis); histopathology; Renal/Kidney: Organ weight;
Comments
related organ weights were appropriate; histopathol- l and did not include this target/organ system.; Re- ive control-related organ weights were appropriate; ely reported and did not include this target/organ sys- trol-related organ weights and serum chemistry pa- athology data were selectively reported and did not
report all information to determine confounding, al- nale controls had decreased body weights and the study y due to animals not receiving water.
rmation either to support or dismiss the suggestion that ups in animal attrition or health outcomes unrelated to ld influence the outcome assessment.
nods of statistical analyses of organ weight and histol- e/Developmental: Appropriate methods of statistical blogy data were used.; Renal/Kidney: Appropriate organ weights, serum chemistry, hematology, and his-
a were adequately presented. Histopathology results not reported. Slides for this tissue/organ system was a NTP Pathology Working Group (PWG). The study ata in which non-neoplastic incidences were observed, y indicate results were negative for other tissues exental: Organ weight data were adequately presented. Sue/organ system were not reported. Slides for this as those reviewed by the NTP Pathology Working pears to report histology data in which non-neoplastic er, the text did not explicitly indicate results were id.; Renal/Kidney: Organ weight and relevant serum resented. Histopathology results for this tissue/organ we in the text, but incidence data were not provided.

HERO ID: 1772371 Table: 4 of 26

<b>Study Citation:</b>	Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).							
Health	ılar/Sensory;							
Outcome(s):								
Reported Health								
Effect(s):				Ocular/Sensory: Histopathology (if grossly abnormal);				
<b>Duration:</b>								
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane							
HERO ID:	1772371							
Domain		Metric	Rating	Comments				
Domain 1: Test Substan								
	Metric 1:	Test Substance Identity	High	All Outcomes: Name, sturcture and CASRN provided				
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source, analytically verified				
	Metric 3:	Test Substance Purity	High	All Outcomes: 99% purity				
Domain 2: Test Design								
C	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Use of vehicle (corn oil) control				
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type				
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers				
Domain 2: Evnagura Ch	peractorization							
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test	High	All Outcomes: Details of preparation were provided. Chemical stability was evaluated;				
	Metric 7.	Substance	riigii	Dose formulations were stable for at least 3 weeks and were appropriately stored for no longer than this time. Samples were analyzed both immediately after mixing and after dosing showing no loss of chemical during dosing administration.				
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: All groups were dosed with a 5mL/kg volume of the test solutions				
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target and analytical dose concentrations and the dose in mg/kg were clearly reported. Formulations were all within 10% of the target concentration, and there was no loss of chemical during dose administration				
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: 5d/week for 13 weeks				
	Metric 11:	Number of Exposure Groups and	High	All Outcomes: 6 dose-groups including controls				
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance				
Domain 4: Test Animals	2							
Domain 4. 16st Allillais	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.				
		Con	tinued on next page	·				

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Study Citation:	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice
Health	(drinking water and gavage studies). Endocrine (Endocrine); Thyroid; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory;
Outcome(s):	
Reported Health	Endocrine (Endocrine): Histology of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.; Thyroid: Related histology;

**Effect(s):** Skin/Connective Tissue: Histology of skin; Musculoskeletal: Related histology; Ocular/Sensory: Histopathology (if grossly abnormal); **Duration:** Subchronic (>30-91 days) 13-week; gavage, F344 Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

1772371			
	Metric	Rating	Comments
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Endocrine (Endocrine): Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.; Thyroid: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.; Skin/Connective Tissue: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.; Musculoskeletal: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.; Ocular/Sensory: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage were not reported.
Metric 15:	Number of Animals per Group	Medium	All Outcomes: 10/sex is appropriate for a rodent subchronic assay
ssessment Metric 16:	Outcome Assessment Methodology	High	Endocrine (Endocrine): Methodology for histology was clearly reported and sensitive for the outcome of interest.; Thyroid: Methodology for histology was clearly reported and sensitive for the outcome of interest.; Skin/Connective Tissue: Methodology for histology was clearly reported and sensitive for the outcome of interest.; Musculoskeletal: Methodology for histology was clearly reported and sensitive for the outcome of interest.; Ocular/Sensory: Animals were observed 2 times daily. Methodology for tissue/organ-related weights and histology was clearly reported and sensitive for the outcome of interest.
Metric 17:	Consistency of Outcome Assessment	High	Endocrine (Endocrine): Details of the outcome assessment protocol for histology were reported and outcomes were assessed consistently across the study groups that were tested (e.g., at the same time after initial exposure) and using the same protocol.; Thyroid: Details of the outcome assessment protocol for histology were reported and outcomes were assessed consistently across the study groups that were tested (e.g., at the same time after initial exposure) and using the same protocol.; Skin/Connective Tissue: Details of the outcome assessment protocol for histology were reported and outcomes were assessed consistently across the study groups that were tested (e.g., at the same time after initial exposure) and using the same protocol.; Musculoskeletal: Details of the outcome assessment protocol for histology were reported and outcomes were assessed consistently across the study groups that were tested (e.g., at the same time after initial exposure) and using the same protocol.; Ocular/Sensory: Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.
	Metric 14:  Metric 15:  ssessment Metric 16:	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group  ssessment Metric 16: Outcome Assessment Methodology	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group Medium  Seessment Metric 16: Outcome Assessment Methodology High

Human Health Hazard Animal Toxicology Evaluation HERO ID: 1772371 Table: 4 of 26

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**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies). Health

**Outcome(s):** 

Endocrine (Endocrine); Thyroid; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory;

Reported Health Endocrine (Endocrine): Histology of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.; Thyroid: Related histology; Skin/Connective Tissue: Histology of skin; Musculoskeletal: Related histology; Ocular/Sensory: Histopathology (if grossly abnormal); Effect(s):

**Duration:** Subchronic (>30-91 days) 13-week; gavage, F344 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

HERO ID:	1772371						
Domain		Metric	Rating	Comments			
	Metric 18:	Sampling Adequacy	Low	Endocrine (Endocrine): Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.; Thyroid: Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided; Skin/Connective Tissue: Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.; Musculoskeletal: Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.; Ocular/Sensory: Histology was done on control and high dose animals only. The results of histological examination are not provided in detail, resulting in uncertainties in whether tissues/organs were affected and preventing an assessment of the appropriateness of doses selected for histopathology examinations (the absence of effects is not explicitly stated). The number of animals evaluated for each organ is also not presented. Therefore, a full assessment of the appropriateness of the number of animals evaluated and the doses selected for histopathology cannot be made.			
	Metric 19: Metric 20:	Blinding of Assessors Negative Control Response	N/A Low	All Outcomes: Not necessary for the outcome of interest.  Endocrine (Endocrine): Negative control responses were not reported.; Thyroid: Negative control responses were not reported.; Skin/Connective Tissue: Negative control responses were not reported.; Musculoskeletal: Negative control responses were not reported.; Ocular/Sensory: Negative control responses were not reported			
Domain 6: Confounding /	Variable Cor	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding, although at week 9, one cage of female controls had decreased body weights and the study authors indicated this was possibly due to animals not receiving water.			
1	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
I	Metric 23:	Data Presentation and Analysis	High	Endocrine (Endocrine): Appropriate methods of statistical analyses of organ weight and histology data were described.; Thyroid: Appropriate methods of statistical analyses of organ weight and histology data were described.; Skin/Connective Tissue: Appropriate methods of statistical analyses of organ weight and histology data were described.; Musculoskeletal: Appropriate methods of statistical analyses of organ weight and histology data were described.; Ocular/Sensory: Appropriate statistical analysis was described.			
-		Cont	inued on next page	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \			

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 1772371 Table: 4 of 26

#### ... continued from previous page

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health Endocrine (Endocrine); Thyroid; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory;

**Outcome(s):** 

Reported Health Endocrine (Endocrine): Histology of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.; Thyroid: Related histology;

Effect(s): Skin/Connective Tissue: Histology of skin; Musculoskeletal: Related histology; Ocular/Sensory: Histopathology (if grossly abnormal);

**Duration:** Subchronic (>30-91 days) 13-week; gavage, F344 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Uninformative	Endocrine (Endocrine): Histopathology results for this organ system were not reported, including no statements indicating whether no effects were observed.; Thyroid: Histopathology results for this organ system were not reported, including no statements indicating whether no effects were observed.; Skin/Connective Tissue: Histopathology results for this organ system were not reported, including no statements indicating whether no effects were observed.; Musculoskeletal: Histopathology results for this organ system were not reported, including no statements indicating whether no effects were observed.; Ocular/Sensory: Histopathology results for this organ/system were not reported including no statements indicating whether no effects were observed.

## **Overall Quality Determination**

HERO ID: 1772371 Table: 5 of 26

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health

Immune/Hematological

**Outcome(s):** 

**Reported Health** 

Histopathology; hematology

Effect(s):

Subchronic (>30-91 days) 13-week; gavage, F344 **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Use of vehicle (corn oil) control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure Cl	naracterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; Dose formulations were stable for at least 3 weeks and were appropriately stored for no longer than this time. Samples were analyzed both immediately after mixing and after dosing showing no loss of chemical during dosing administration.
	Metric 8:	Consistency of Exposure	High	All groups were dosed with a 5mL/kg volume of the test solutions
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Target and analytical dose concentrations and the dose in mg/kg were clearly reported. Formulations were all within 10% of the target concentration, and there was no loss of chemical during dose administration
	Metric 10:	Exposure Frequency and Duration	High	5d/week for 13 weeks
	Metric 11:	Number of Exposure Groups and	High	6 dose-groups including controls
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex is appropriate for a rodent subchronic assay; 20 males were used for some groups to be used for hematology/clinical chemistry
Domain 5: Outcome As	esesement			
Domain 3. Outcome As	Metric 16:	Outcome Assessment Methodology	High	Methodology for clinical chemistry and for tissue/organ-related weights and histology was clearly reported and sensitive for the outcome of interest.

HERO ID: 1772371 Table: 5 of 26

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Study Citation:	itation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6 (drinking water and gavage studies).								
Health	Immune/Hematological								
Outcome(s):	inimule/Tenacological								
Reported Health	Histopatholo	ogy; hematology							
Effect(s):	more	ygj, nomucologj							
Duration:	Subchronic	(>30-91 days) 13-week; gavage, F344							
Chemical:		bethane- Isomer: 1,2-Dichloroethane							
HERO ID:	1772371								
Domain		Metric	Rating	Comments					
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol for organ weights and histology were reported and outcomes were assessed consistently across study groups that were being assessed (e.g., at the same time after initial exposure) using the same protocol for groups included in the assessment.					
	Metric 18:	Sampling Adequacy	Low	Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females; Clinical chemistry and hematology was performed on males only, and only in the top 3 dose groups. Since all males in the highest group died, serum chemistry was only available for the 120 and 240 dose groups. The number of samples available at the collection timepoints varied, from 3 to 9 animals. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.					
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.					
	Metric 20:	Negative Control Response	Medium	Negative control responses appeared to be appropriate but histopathology data were not reported for spleen, thymus, and lymph nodes.					
Domain 6: Confoundin	ng / Variable Co	ntrol							
Domain o. Comounan	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding, although at week 9, one cage of female controls had decreased body weights and the study authors indicated this was possibly due to animals not receiving water.					
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.					
	Metric 23:	Data Presentation and Analysis	High	Appropriate methods of statistical analyses of organ weights, serum chemistry, hematology, and histology data were used.					
	Metric 24:	Reporting of Data	Medium	Organ weight and relevant serum chemistry data were adequately presented. Histopathology results for this tissue/organ system were reported with incidences. Histopathology data were not reported for spleen, thymus, and lymph nodes.					

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Domain 5: Outcome Assessment

Metric 16:

Outcome Assessment Methodology

NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice **Study Citation:** (drinking water and gavage studies). Health Gastrointestinal Outcome(s): **Reported Health** Histopathology Effect(s): **Duration:** Subchronic (>30-91 days) 13-week; gavage, F344 Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1772371 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Name, sturcture and CASRN provided Metric 2: Test Substance Source High Commercial source, analytically verified Metric 3: Test Substance Purity High 99% purity Domain 2: Test Design Negative and Vehicle Controls Metric 4: High Use of vehicle (corn oil) control Metric 5: Positive Controls N/A Not necessary for the study type Metric 6: Randomized Allocation of Animals Medium Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers Domain 3: Exposure Characterization Preparation and Storage of Test Metric 7: High Details of preparation were provided. Chemical stability was evaluated; Dose formulations were stable for at least 3 weeks and were appropriately stored for no longer than Substance this time. Samples were analyzed both immediately after mixing and after dosing showing no loss of chemical during dosing administration. Metric 8: Consistency of Exposure High All groups were dosed with a 5mL/kg volume of the test solutions Administration Reporting of Doses/Concentrations Metric 9: High Target and analytical dose concentrations and the dose in mg/kg were clearly reported. Formulations were all within 10% of the target concentration, and there was no loss of chemical during dose administration Metric 10: Exposure Frequency and Duration High 5d/week for 13 weeks Number of Exposure Groups and Metric 11: High 6 dose-groups including controls Dose/Concentration Spacing Metric 12: Exposure Route and Method High The route and method of exposure were reported and were suited to the test substance Domain 4: Test Animals Metric 13: Test Animal Characteristics High Species, strain, sex, age, source and initial BW were reported and were appropriate. Metric 14: Adequacy and Consistency of Animal Medium Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported. **Husbandry Conditions** Metric 15: Number of Animals per Group Medium 10/sex is appropriate for a rodent subchronic assay

est.

High

Methodology for histology was clearly reported and sensitive for the outcome of inter-

### ... continued from previous page

Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health

Gastrointestinal

Outcome(s):

**Reported Health** 

Histopathology

Effect(s):

**Duration:** Subchronic (>30-91 days) 13-week; gavage, F344 **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Low	Although it is acceptable to perform histology in only the high-dose group and control group when no effects are observed at the high dose (e.g., see OECD 409), the results of histological examination are not provided in detail for each organ, resulting in uncertainties in whether tissues/organs were affected and preventing an assessment of the appropriateness of doses selected for histopathology examinations. The number of animals evaluated for each organ is also not presented. Therefore, a full assessment of the appropriateness of the number of animals evaluated for each organ and the doses selected for histopathology cannot be made.
	Metric 18:	Sampling Adequacy	Low	Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	High	Negative control-related organ weights and histology reported for this outcome were appropriate.
Domain 6: Confounding	g / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding, although at week 9, one cage of female controls had decreased body weights and the study authors indicated this was possibly due to animals not receiving water.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Appropriate methods of statistical analyses of organ weight and histology data were described.
	Metric 24:	Reporting of Data	High	Histopathology results for this tissue/organ system were reported with incidences.

## **Overall Quality Determination**

## High

,1-Dichloroethane	Human Health Hazard Animal Toxicology Evaluation	HERO ID: 1772371 Table: 7 of 26
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**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies). Neurological/Behavioral Health

**Outcome(s):** 

**Reported Health** 

Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea

Effect(s):

Subchronic (>30-91 days) 13-week; gavage, F344 **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

	1772371			
Domain		Metric	Rating	Comments
Domain 1: Test Substar	ice			
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Use of vehicle (corn oil) control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure Cl	naracterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; Dose formulations were stable for at least 3 weeks and were appropriately stored for no longer than this time. Samples were analyzed both immediately after mixing and after dosing showing no loss of chemical during dosing administration.
	Metric 8:	Consistency of Exposure	High	All groups were dosed with a 5mL/kg volume of the test solutions
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Target and analytical dose concentrations and the dose in mg/kg were clearly reported. Formulations were all within 10% of the target concentration, and there was no loss of chemical during dose administration
	Metric 10:	Exposure Frequency and Duration	High	5d/week for 13 weeks
	Metric 11:	Number of Exposure Groups and	High	6 dose-groups including controls
		Dose/Concentration Spacing	8	
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent
		Husbandry Conditions		between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex is appropriate for a rodent subchronic assay
Domain 5: Outcome As	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	Animals were observed 2 times daily. Methodology for tissue/organ-related weights and histology was clearly reported and sensitive for the outcome of interest.

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Study Citation:	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).						
Health	Neurological/Behavioral						
Outcome(s):							
Reported Health	Histopatholo	ogy; organ weight (brain), clinical signs incl	luded tremor	rs, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea			
Effect(s):							
Duration:		(>30-91 days) 13-week; gavage, F344					
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	1772371						
Domain		Metric	Rating	Comments			
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of observations of behavioral clinical signs (e.g., timing of assessment across groups) were not reported. Details of the outcome assessment protocol for organ weights and histology were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol for groups included in the assessment.			
	Metric 18:	Sampling Adequacy	Low	Details for sampling for bevioral clinical signs were not provided. Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females.			
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.			
	Metric 20:	Negative Control Response	Medium	The biological responses for behavioral clinical signs were not reported for the negative control group(s). Negative control-related organ weights were appropriate			
Domain 6: Confoundir	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding, although at week 9, one cage of female controls had decreased body weights and the study authors indicated this was possibly due to animals not receiving water.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	Low	Appropriate methods of statistical analyses of organ weight and histology data were used. Behavioral clinical signs data were not statistically analyzed and this data were not provided for independent review.			
	Metric 24:	Reporting of Data	Medium	Results of clinical signs were described in text for some, but not all dose groups without indication of statistical significance; quantal data were not provided for an independent analysis. Organ weight and histology data were adequately presented.			

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**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).

Health

Lung/Respiratory

**Outcome(s):** 

**Reported Health** 

Organ weight, histopathology

Effect(s):

Subchronic (>30-91 days) 13-week; gavage, F344 **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Substar				
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Design				
_	Metric 4:	Negative and Vehicle Controls	High	Use of vehicle (corn oil) control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure Cl	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; Dose formulations were stable for at least 3 weeks and were appropriately stored for no longer than this time. Samples were analyzed both immediately after mixing and after dosing showing no loss of chemical during dosing administration.
	Metric 8:	Consistency of Exposure Administration	High	All groups were dosed with a 5mL/kg volume of the test solutions
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical dose concentrations and the dose in mg/kg were clearly reported. Formulations were all within 10% of the target concentration, and there was no loss of chemical during dose administration
	Metric 10:	Exposure Frequency and Duration	High	5d/week for 13 weeks
	Metric 11:	Number of Exposure Groups and	High	6 dose-groups including controls
		Dose/Concentration Spacing	_	
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance
Domain 4: Test Animal	ls			
20	Metric 13:	Test Animal Characteristics	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex is appropriate for a rodent subchronic assay
Domain 5: Outages A				
Domain 5: Outcome As	Metric 16:	Outcome Assessment Methodology	High	Methodology for tissue/organ-related weights and histology was clearly reported and sensitive for the outcome of interest.
		Contin	nued on nex	at page

		contin	ued from p	revious page					
Study Citation:	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).								
Health Outcome(s):		Lung/Respiratory							
Reported Health Effect(s):	Organ weigh	Organ weight, histopathology							
Duration:	Subchronic (	(>30-91 days) 13-week; gavage, F344							
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1772371								
Domain		Metric	Rating	Comments					
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol for organ weights and histology were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol for groups included in the assessment.					
	Metric 18:	Sampling Adequacy	Low	Histological analysis was not performed on all dose groups, or in the same number of dose groups between males and females. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.					
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.					
	Metric 20:	Negative Control Response	Low	Negative control-related organ weights were appropriate; histopathology data were selectively reported and did not include this target/organ system.					
Domain 6: Confoundin	ng / Variable Co	ntrol							
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding, although at week 9, one cage of female controls had decreased body weights and the study authors indicated this was possibly due to animals not receiving water.					
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.					
	Metric 23:	Data Presentation and Analysis	High	Appropriate methods of statistical analyses of organ weight and histology data were used.					
	Metric 24:	Reporting of Data	Low	Organ weight data were adequately presented. Histopathology results for this tissue/organ system were not reported. Slides for this tissue/organ system was not listed as those reviewed by the NTP Pathology Working Group (PWG). The study only appears to report histology data in which non-neoplastic incidences were observed, however, the text did not explicitly indicate results were negative for other tissues examined.					

## **Overall Quality Determination**

## High

Human Health Hazard Animal Toxicology Evaluation 1,1-Dichloroethane HERO ID: 1772371 Table: 9 of 26

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health

Thyroid

**Outcome(s):** 

**Reported Health** Related histology

Effect(s):

Subchronic (>30-91 days) 13-weeks; drinking water; rats **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Desig	n			
C	Metric 4:	Negative and Vehicle Controls	High	Water only control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Anim	als			
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.

#### Domain 5: Outcome Assessment

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**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).

Health Thyroid

Outcome(s):

Reported Health

Related histology

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain	Metric		Comments
Metric 16:	Outcome Assessment Methodology	High	Outcome assessment was limited to histology, but OECD 409 does not require additional endpoints to be measured for these outcomes.
Metric 17:	Consistency of Outcome Assessment	High	Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.
Metric 18:	Sampling Adequacy	Low	Histology was done on control and high dose animals only. The number of animals eval- uated histologically for each organ is unclear because a full presentation of histological results is not provided.
Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.
Metric 20:	Negative Control Response	Low	The biological responses of the negative control group(s) were not reported.
Domain 6: Confounding / Variable C	ontrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 70% decrease in water intake at the highest dose. This was reported to result in dehydration which could have an impact on study results
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	High	Appropriate statistical analysis was described for organ weight and histopathology
Metric 24:	Reporting of Data	Uninformative	Histopathology results for this organ/system were not reported

## **Overall Quality Determination**

(drinking water and gavage studies). Mortality

Health

**Outcome(s):** 

**Reported Health** 

Survival

Effect(s):

Subchronic (>30-91 days) 13-Week; Drinking water; mice **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

HERO ID.	1772371			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Water only control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure Ch	aracterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure Administration	High	Animals had access to drinking water ad libitum, however, the number of animals per cage was not reported.
	Metric 9:	Reporting of Doses/Concentrations	Low	Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Animals	8			
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex/dose
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	High	Animals were observed for mortality
		Contin	nued on nex	xt page

## Human Health Hazard Animal Toxicology Evaluation

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**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies). Health

**Outcome(s):** 

Mortality

**Reported Health** 

Survival

Effect(s): **Duration:** 

Subchronic (>30-91 days) 13-Week; Drinking water; mice

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

1772371 **HERO ID:** 

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	High	Animals from all groups were consistently observed for this endpoint.
	Metric 18:	Sampling Adequacy	High	All animals were assessed for this endpoint
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.
	,		The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).	
Domain 6: Confound	ing / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Food intake was not reported. There was reported variation in drinking water intake from week to week during the study, and uncertainty in how intakes varied across the groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed for this outcome, but sufficient data as provided to conduct independent analysis.
	Metric 24:	Reporting of Data	High	Survival data were clearly reported for all groups including controls.

# **Overall Quality Determination**

## High

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**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies). Nutritional/Metabolic Health

**Outcome(s):** 

**Reported Health** 

Body weight, weight gain, water consumption

Effect(s):

Subchronic (>30-91 days) 13-Week; Drinking water; mice **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	Water only control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure Ch	paracterization			
20 21. 2poo 2	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex/group

#### Domain 5: Outcome Assessment

		contin	ued from p	revious page			
Study Citation:		. Toxicity studies of 1,2-dichloroethane (et ater and gavage studies).	hylene bichl	oride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mid			
Health	Nutritional/N						
Outcome(s):							
Reported Health	Body weight, weight gain, water consumption						
Effect(s):							
<b>Duration:</b>	Subchronic (	(>30-91 days) 13-Week; Drinking water; m	ice				
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	1772371						
Domain		Metric	Rating	Comments			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.			
	Metric 17:	Consistency of Outcome Assessment	High	Exposed and control animals were consistently observed for this outcome.			
	Metric 18:	Sampling Adequacy	High	Body weight and water consumption appeared to be measured in all surviving animals in each dose group.			
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.			
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group(s) were adequately reported			
Domain 6: Confoundin	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Food intake was not reported. There was reported variation in drinking water intake from week to week during the study, and uncertainty in how intakes varied across the groups.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	Appropriate statistical analysis was used to evaluate body weights. Growth curves were not statistically analyzed, but data were reported allowing for independent review.			
	Metric 24:	Reporting of Data	Low	The results for body weights and change were adequately reported (e.g., means $\pm$ SD). Growth curves data graphically displayed (in the absence of statistical analysis). However, there was a lack in the reporting of the variability in the water intake data.			

NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

HERO ID: 1772371 Table: 12 of 26

(drinking water and gavage studies).

Health

Mortality

**Outcome(s):** 

**Study Citation:** 

**Reported Health** Survival

Effect(s):

**Duration:** 

Subchronic (>30-91 days) 13-weeks; drinking water; rats

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Design	1			
C	Metric 4:	Negative and Vehicle Controls	High	Water only control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure C	'haracterization			
Domain J. Exposure C	Metric 7:	Preparation and Storage of Test	High	Details of preparation were provided. Chemical stability was evaluated; stability studies
	1/10/11/0 / /	Substance	111811	were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported
	Metric 15:	Number of Animals per Group	Medium	10/sex for main group, an additional 10 males/sex for hematology and clinical chemistry.

#### Domain 5: Outcome Assessment

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Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health

Mortality

**Outcome**(s):

Reported Health

Survival

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	High	Animals were observed for mortality
	Metric 17:	Consistency of Outcome Assessment	High	Animals from all groups were consistently observed for this endpoint.
	Metric 18:	Sampling Adequacy	High	All animals were assessed for this endpoint
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 70% decrease in water intake at the highest dose. This was reported to result in dehydration which was reflected in hematology and serum chemistry and organ weight results.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed for this outcome, but sufficient data as provided to conduct independent analysis.
	Metric 24:	Reporting of Data	High	Survival data were clearly reported for all groups including controls.

## **Overall Quality Determination**

HERO ID: 1772371 Table: 13 of 26

NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice **Study Citation:** (drinking water and gavage studies). Health Nutritional/Metabolic Outcome(s): Reported Health Body weight, weight gain, water consumption Effect(s): **Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1772371 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Name, sturcture and CASRN provided Metric 2: Test Substance Source High Commercial source, analytically verified Metric 3: Test Substance Purity High 99% purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High Water only control N/A Metric 5: Positive Controls Not necessary for the study type Metric 6: Medium Randomized Allocation of Animals Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers Domain 3: Exposure Characterization Preparation and Storage of Test Metric 7: High Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water Substance replaced daily). Consistency of Exposure High Metric 8: Test substance was administered consistently across study groups Administration Reporting of Doses/Concentrations Metric 9: Low Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity. Metric 10: **Exposure Frequency and Duration** High Continuously via drinking water for 13-weeks Number of Exposure Groups and Metric 11: High 6 dose-groups including controls; doses selected were influenced by solubility being a Dose/Concentration Spacing limiting factor. Exposure Route and Method Metric 12: Low The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing. Domain 4: Test Animals Metric 13: Test Animal Characteristics High Species, strain, sex, age, source and initial BW were reported and were appropriate. Metric 14: Adequacy and Consistency of Animal Medium Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported. **Husbandry Conditions** Metric 15: Number of Animals per Group Medium 10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry. Domain 5: Outcome Assessment

		cor	ntinued from previous	page				
Study Citation:		. Toxicity studies of 1,2-dichloroethane (ethylter and gavage studies).	lene bichloride) in F34	4/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice				
Health	Nutritional/N							
Outcome(s):								
Reported Health	Body weigh	t, weight gain, water consumption						
Effect(s):		,,g g,						
Duration:	Subchronic (>30-91 days) 13-weeks; drinking water; rats							
Chemical:		1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	1772371	2000001 1,2 2100000000000000000000000000						
Domain		Metric	Rating	Comments				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.				
	Metric 17:	Consistency of Outcome Assessment	High	Exposed and control animals were consistently observed for this outcome.				
	Metric 18:	Sampling Adequacy	High	Body weight and water consumption appeared to be measured in all surviving animals in each dose group				
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.				
	Metric 20:	Negative Control Response	High	There are no apparent deficiencies for this outcome for negative control response report ing.				
Domain 6: Confoundi	ing / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 60% decrease in water intake at the highest dose. This was reported to result in dehydration which was reflected in hematology and serun chemistry and organ weight results.				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.				
	Metric 23:	Data Presentation and Analysis	High	Appropriate statistical analysis was used to evaluate body weights. Growth curves were not statistically analyzed, but data were reported allowing for independent review.				
	Metric 24:	Reporting of Data	Low	The results for body weights and change were adequately reported (e.g., means $\pm$ SD). Growth curves data graphically displayed (in the absence of statistical analysis). However, the variability in the water intake data was not reported.				

# **Overall Quality Determination**

Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).

Health

Lung/Respiratory; Cardiovascular; Reproductive/Developmental;

Outcome(s): Reported Health

Lung/Respiratory: Organ weight, histopathology; Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight

HERO ID: 1772371 Table: 14 of 26

**Effect(s):** (Testis); histopathology;

**Duration:** Subchronic (>30-91 days) 13-Week; Drinking water; mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain 1: Test Substance  Metric 1: Test Substance Identity Metric 2: Test Substance Source Metric 3: Test Substance Source Metric 3: Test Substance Purity Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals Metric 6: Randomized Allocation of Animals Metric 6: Randomized Allocation of Animals Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration Reporting of Doses/Concentrations Metric 9: Metric 9: Exposure Frequency and Duration Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups Metric 12: Test Animals Metric 13: Test Animals Metric 14: Adequacy and Consistency of Animal Metric 15: Number of Animals per Group Metric 15: Number of Animals per Group Metric 15: Number of Animals per Group Medium Medium All Outcomes: Same, sturcture and CASRN provided All Outcomes: Commercial source, analytically verified All Outcomes: Meter only control All Outcomes: Not necessary for the study type All Outcomes: Animals All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, neasures were taken to minimize looses for manumers and to groups administered consistently across study groups All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the minimized concentration and the concentration found at the end of 24 hrs leading to some ambiguity.  All Outcomes: Out	Domain		Metric	Rating	Comments
Metric 2: Test Substance Source   High All Outcomes: Commercial source, analytically verified   All Outcomes: 99% purity	Domain 1: Test Substance	ce			
Domain 2: Test Design Metric 4: Negative and Vehicle Controls Metric 6: Randomized Allocation of Animals Medium  Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance  Domain 3: Exposure Characterization Metric 8: Consistency of Exposure  Metric 9: Reporting of Doses/Concentrations Metric 9: Reporting of Doses/Concentrations  Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 13: Test Animals  Metric 13: Test Animals  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium All Outcomes: Species, strain, sex, age, source and initial BW were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.  Medium All Outcomes: Too water only control weight the study type  All Outcomes: Water only control  All Outcomes: Water only control  All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability subles were performed, and based on results, measures and then assigned to each study to eight classes and then assigned to each stability was evaluated; stability studies were performed, and Durcomes: Test substance was administered consistent between exposed and control groups. The number of animals per cage was not preparation were provided. Chemical stability was evaluated; All Ou		Metric 1:	Test Substance Identity	High	All Outcomes: Name, sturcture and CASRN provided
Domain 2: Test Design  Metric 4: Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance  Metric 9: Metric 9: Preparation and Storage of Test Metric 9: Preparation and Storage of Test Metric 9: All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).  Metric 9: All Outcomes: Test substance was administered consistently across study groups  All Outcomes: Test substance was administered consistently across study groups  All Outcomes: Test substance was administered concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentration and the concentration and the concentration and the concentration and the concentration found at the end of 24 hrs leading to some ambiguity.  Metric 10: Exposure Frequency and Duration Metric 12: Exposure Route and Method  Dose/Concentration Spacing Metric 13: Test Animals  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium  All Outcomes: Species, strain, sex, age, source and initial BW were reported to be consistent beveen exposed and control groups. The number of animals per cage was not reported.		Metric 2:	Test Substance Source	High	All Outcomes: Commercial source, analytically verified
Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls N/A Medium All Outcomes: Water only control Whetic 5: Positive Controls N/A All Outcomes: Not necessary for the study type  Metric 6: Randomized Allocation of Animals Medium All Outcomes: Not necessary for the study type  All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups byanother table of random numbers  Metric 7: Preparation and Storage of Test Substance  Preparation and Storage of Test Substance Preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).  Metric 8: Consistency of Exposure  Metric 9: Reporting of Doses/Concentrations  Metric 9: All Outcomes: Test substance was administered consistently across study groups  All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.  Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method Low All Outcomes: Continuously via drinking water for 13-weeks  Metric 13: Test Animal Characteristics High All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported to be consistent between exposed and control groups. The number of anim		Metric 3:	Test Substance Purity	High	All Outcomes: 99% purity
Metric 5: Metric 6: Randomized Allocation of Animals Medium All Outcomes: Not necessary for the study type All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups byanother table of random numbers dable of random numbers and to groups byanother table	Domain 2: Test Design				
Metric 6: Randomized Allocation of Animals  Medium All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups byanother table of random numbers  Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure High All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).  Metric 9: Reporting of Doses/Concentrations  Metric 9: Reporting of Doses/Concentrations  Metric 10: Exposure Frequency and Duration High All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentration found at the end of 24 hrs leading to some ambiguity.  Metric 10: Exposure Frequency and Duration High All Outcomes: Continuously via drinking water for 13-weeks Dose/Concentration Spacing High All Outcomes: Outinuously via drinking water for 13-weeks olosse-groups including controls; doses selected were influenced by solubility being a limiting factor.  All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium All Outcomes: Tenp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.		Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Water only control
Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration Reporting of Doses/Concentrations  Metric 9: Metric 9: Metric 10: Metric 10: Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Metric 12:  Domain 4: Test Animals  Metric 13:  Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium  All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).  All Outcomes: Test substance was administered consistently across study groups  All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration of 24 hrs leading to some ambiguity.  All Outcomes: Continuously via drinking water for 13-weeks All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.  All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.		Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
Metric 7: Preparation and Storage of Test Substance Substance  Metric 8: Consistency of Exposure High All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).  Metric 8: Consistency of Exposure High All Outcomes: Test substance was administered consistently across study groups  Administration Reporting of Doses/Concentrations  Low All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration found at the end of 24 hrs leading to some ambiguity.  Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing High All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.  Metric 12: Exposure Route and Method Low All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.		Metric 6:	Randomized Allocation of Animals	Medium	
Metric 7: Preparation and Storage of Test Substance Substance  Metric 8: Consistency of Exposure High All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).  Metric 8: Consistency of Exposure High All Outcomes: Test substance was administered consistently across study groups  Administration Reporting of Doses/Concentrations  Low All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration found at the end of 24 hrs leading to some ambiguity.  Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing High All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.  Metric 12: Exposure Route and Method Low All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.	Domain 3: Exposure Ch.	aracterization			
Metric 9: Administration Reporting of Doses/Concentrations  Low All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.  Metric 10: Exposure Frequency and Duration High All Outcomes: Continuously via drinking water for 13-weeks Metric 11: Number of Exposure Groups and Dose/Concentration Spacing All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.  Metric 12: Exposure Route and Method Low All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.	· · · · · · · · · · · · · · · · · · ·			High	stability studies were performed, and based on results, measures were taken to minimize
Metric 9: Reporting of Doses/Concentrations    Low   All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.    Metric 10: Exposure Frequency and Duration   High   All Outcomes: Continuously via drinking water for 13-weeks   Metric 11: Number of Exposure Groups and Dose/Concentration Spacing   Low   All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.    Metric 12: Exposure Route and Method   Low   All Outcomes: Target and determined concentrations were reported were influenced between the initial concentration and the concentration and the concentration found at the end of 24 hrs leading to some ambiguity.    All Outcomes: Continuously via drinking water for 13-weeks   All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.    All Outcomes: Target and determined concentrations water for 13-weeks   All Outcomes: Target and determined concentrations to some ambiguity.    All Outcomes: Target and determined concentrations that the end of 24 hrs leading to some ambiguity.    All Outcomes: Target and determined concentrations, thus animals exposed concentrations tanged between the initial concentration and the concentration of the tween the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.    All Outcomes: Target and determined concentration found at the end of 24 hrs leading to some ambiguity.    All Outcomes: Target and determined concentration found at the end of 24 hrs leading to some ambiguity.    All Outcomes: Target and determined concentration found at the end of 24 hrs leading to some ambiguity.    All Outcomes: Target and determined t		Metric 8:	J 1	High	All Outcomes: Test substance was administered consistently across study groups
Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Domain 4: Test Animals  Metric 13: Test Animals  Metric 14: Adequacy and Consistency of Animal High All Outcomes: Continuously via drinking water for 13-weeks All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.  Low All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.		Metric 9:		Low	of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading
Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Dose/Concentration Spacing Metric 12: Exposure Route and Method  Dose/Concentration Spacing Metric 13: Test Animals  Metric 13: Test Animal Characteristics Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium High All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.  All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  Medium All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.		Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Continuously via drinking water for 13-weeks
Metric 12: Exposure Route and Method  Low All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.  Domain 4: Test Animals  Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium Husbandry Conditions  Medium All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.		Metric 11:		High	All Outcomes: 6 dose-groups including controls; doses selected were influenced by
Metric 13: Test Animal Characteristics  High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium Husbandry Conditions  High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.  All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.		Metric 12:		Low	All Outcomes: The exposure route proved challenging due to the volatility of the test
Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Adequacy and Consistency of Animal Husbandry Conditions  All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.	Domain 4: Test Animals				
Husbandry Conditions consistent between exposed and control groups. The number of animals per cage was not reported.		Metric 13:	Test Animal Characteristics	High	
Metric 15: Number of Animals per Group Medium All Outcomes: 10/sex/group		Metric 14:	1 3	Medium	consistent between exposed and control groups. The number of animals per cage was
		Metric 15:	Number of Animals per Group	Medium	All Outcomes: 10/sex/group

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Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health Lung/Respiratory; Cardiovascular; Reproductive/Developmental;

**Outcome**(s):

Reported Health Lung/Respiratory: Organ weight, histopathology; Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight

**Effect(s):** (Testis); histopathology;

**Duration:** Subchronic (>30-91 days) 13-Week; Drinking water; mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Exposed and control animals were consistently observed for this outcome.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Organ weights were measured for all surviving main group animals; Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight)
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Lung/Respiratory: Food intake was not reported. There was reported variation in drinking water intake from week to week during the study, and uncertainty in how intakes varied across the groups.; Cardiovascular: Water intake between exposed and control animals was comparable. Food intake was not reported.; Reproductive/Developmental: Food intake was not reported. There was reported variation in drinking water intake from week to week during the study, and uncertainty in how intakes varied across the groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Appropriate statistical analysis was described for organ weight and histopathology
	Metric 24:	Reporting of Data	Low	All Outcomes: Relevant organ weights were adequately reported. Histopathology results for this outcome were not reported.

## **Overall Quality Determination**

## Medium

HERO ID: 1772371 Table: 15 of 26

<b>Study Citation:</b>		•	ne bichloride) in F3	44/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice	
Health		tter and gavage studies).	orina (Endaarina ara	cana), Skin/Cannactiva Tissua (Endacrina argana), Gastraintectinal	
Outcome(s):	Ocular/Sensory; Musculoskeletal (Endocrine organs); Endocrine (Endocrine organs); Skin/Connective Tissue (Endocrine organs); Gastrointestinal;				
Reported Health Ocular/Sensory: Histopathology (if grossly abnormal); Musculoskeletal (Endocrine organs): Related histology; Endocrine (Endocrine organs): Histology					
Effect(s):			Could also include p	pancreas.; Skin/Connective Tissue (Endocrine organs): Histology of skin;	
Duration:	Subchronic (	nal: Histopathology; (>30-91 days) 13-Week; Drinking water; mice			
Chemical:		bethane- Isomer: 1,2-Dichloroethane			
	1772371	ethane- isomer. 1,2-Diemoroethane			
Domain		Metric	Rating	Comments	
Domain 1: Test Substance	<u> </u>		&		
	Metric 1:	Test Substance Identity	High	All Outcomes: Name, sturcture and CASRN provided	
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source, analytically verified	
	Metric 3:	Test Substance Purity	High	All Outcomes: 99% purity	
Domain 2: Test Design					
C	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Water only control	
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type	
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assigned to cages by one	
				table of random numbers and to groups byanother table of random numbers	
Domain 3: Exposure Char	rootorization				
_	Metric 7:	Preparation and Storage of Test	High	All Outcomes: Details of preparation were provided. Chemical stability was evaluated;	
	wietric 7.	Substance	mgn	stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).	
	Metric 8:	Consistency of Exposure Administration	High	Ocular/Sensory: Test substance was administered consistently across study groups; Musculoskeletal (Endocrine organs): The outcome assessment methods for this organ/system were limited because hematology and clinical chemistry measurements were not conducted in the mouse study.; Endocrine (Endocrine organs): Test substance was administered consistently across study groups; Skin/Connective Tissue (Endocrine organs): Test substance was administered consistently across study groups; Gastrointestinal: Test substance was administered consistently across study groups	
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.	
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Continuously via drinking water for 13-weeks	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.	
	Metric 12:	Exposure Route and Method	Low	All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.	
Domain 4: Test Animals		Cont	inued on next page		

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		cont	inued from previou	s page				
Study Citation:	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).							
Health		Ocular/Sensory; Musculoskeletal (Endocrine organs); Endocrine (Endocrine organs); Skin/Connective Tissue (Endocrine organs); Gastrointestinal;						
Outcome(s):								
Reported Health	Ocular/Sens	Ocular/Sensory: Histopathology (if grossly abnormal); Musculoskeletal (Endocrine organs): Related histology; Endocrine (Endocrine organs): Histology of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.; Skin/Connective Tissue (Endocrine organs): Histology of skin;						
Effect(s):	of related tis	sues/organs (Adrenal glands, pituitary gland).	Could also include p	pancreas.; Skin/Connective Tissue (Endocrine organs): Histology of skin;				
		inal: Histopathology;						
Duration:		(>30-91 days) 13-Week; Drinking water; mice						
Chemical:		bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	1772371							
Domain		Metric	Rating	Comments				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.				
	Metric 15:	Number of Animals per Group	Medium	Ocular/Sensory: 10/sex/group; Musculoskeletal (Endocrine organs): 10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.; Endocrine (Endocrine organs): 10/sex/group; Skin/Connective Tissue (Endocrine organs): 10/sex/group.; Gastrointestinal: 10/sex/group				
D								
Domain 5: Outcome			TT: 1					
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.				
	Metric 17:	Consistency of Outcome Assessment	High	Ocular/Sensory: Exposed and control animals were consistently observed for this outcome.; Musculoskeletal (Endocrine organs): Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.; Endocrine (Endocrine organs). Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.; Skin/Connective Tissue (Endocrine organs): Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.; Gastrointestina Exposed and control animals were consistently observed for this outcome.				
	Metric 18:	Sampling Adequacy	Low	Ocular/Sensory: Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.; Musculoskeletal (Endocrine organs): Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological result is not provided.; Endocrine (Endocrine organs): Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided; Skin/Connective Tissue (Endocrine organs): Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.; Gastrointestinal: Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.				
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		cor	ntinued from previous	page				
Study Citation:		NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).						
Health			ocrine (Endocrine organ	ns); Skin/Connective Tissue (Endocrine organs); Gastrointestinal;				
Outcome(s):			`					
Reported Health	Ocular/Sens	cular/Sensory: Histopathology (if grossly abnormal); Musculoskeletal (Endocrine organs): Related histology; Endocrine (Endocrine organs): Histology						
Effect(s):	of related tis	of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.; Skin/Connective Tissue (Endocrine organs): Histology of skin;						
	Gastrointest	inal: Histopathology;	_					
<b>Duration:</b>		Subchronic (>30-91 days) 13-Week; Drinking water; mice						
Chemical:	1,1-Dichloro	pethane- Isomer: 1,2-Dichloroethane						
HERO ID:	1772371							
Domain		Metric	Rating	Comments				
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological responses of the negative control group(s) were not reported.				
Domain 6: Confound	ing / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Food intake was not reported. There was reported variation in drinking water intake from week to week during the study, and uncertainty in how intakes varied across the groups.				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Appropriate statistical analysis was described for organ weight and histopathology				
	Metric 24:	Reporting of Data	Uninformative	Ocular/Sensory: Histopathology results for this organ/system were not reported.; Musculoskeletal (Endocrine organs): Histopathology results for this organ/system were not reported; Endocrine (Endocrine organs): Histopathology results for this organ/system were not reported; Skin/Connective Tissue (Endocrine organs): Histopathology results for this organ/system were not reported; Gastrointestinal: Histopathology results for this organ/system were not reported.				

# **Overall Quality Determination**

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 1772371 Table: 16 of 26

Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health Neurological/Behavioral

**Outcome(s):** 

Reported Health Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea

Effect(s):

**Duration:** Subchronic (>30-91 days) 13-Week; Drinking water; mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Desi	gn			
	Metric 4:	Negative and Vehicle Controls	High	Water only control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure	Characterization			
Boniani 5. Exposure	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex/group

#### Domain 5: Outcome Assessment

## Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

Study Citation:

NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).

Health

Neurological/Behavioral

**Outcome(s):** 

Reported Health

Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea

Effect(s):
Duration:

Subchronic (>30-91 days) 13-Week; Drinking water; mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Exposed and control animals were consistently observed for this outcome.
	Metric 18:	Sampling Adequacy	Low	Histology was done on control and high dose animals only. The sampling adequacy of clinical signs is uncertain because incidence data were not reported. Organ weight sampling was adequate. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Low	The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight)
Domain 6: Confound	ing / Variable Co Metric 21:	Confounding Variables in Test Design	Low	Food intake was not reported. There was reported variation in drinking water intake
		and Procedures		from week to week during the study, and uncertainty in how intakes varied across the groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Appropriate statistical analysis was described for organ weight and histopathology. Statistical analysis was not described for clinical signs, and these data were not provided for independent review.
	Metric 24:	Reporting of Data	Low	Relevant organ weight was adequately reported. Results of clinical observations were described in the text as negative. Histopathology results for this outcome were not reported.

## **Overall Quality Determination**

## Medium

HERO ID: 1772371 Table: 17 of 26

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**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies). Health Reproductive/Developmental; Lung/Respiratory; Outcome(s): Reported Health Reproductive/Developmental: Organ weight (Testis); histopathology; Lung/Respiratory: Organ weight, histopathology; Effect(s): **Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1772371 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: High Test Substance Identity All Outcomes: Name, sturcture and CASRN provided Metric 2: Test Substance Source High All Outcomes: Commercial source, analytically verified Metric 3: Test Substance Purity High All Outcomes: 99% purity Domain 2: Test Design Negative and Vehicle Controls Metric 4: High All Outcomes: Water only control Metric 5: Positive Controls N/A All Outcomes: Not necessary for the study type Metric 6: Medium Randomized Allocation of Animals All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test High All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize Substance losses (water replaced daily). Metric 8: Consistency of Exposure High All Outcomes: Test substance was administered consistently across study groups Administration Reporting of Doses/Concentrations Metric 9: Low All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity. Metric 10: **Exposure Frequency and Duration** High All Outcomes: Continuously via drinking water for 13-weeks Number of Exposure Groups and Metric 11: High All Outcomes: 6 dose-groups including controls; doses selected were influenced by Dose/Concentration Spacing solubility being a limiting factor. Exposure Route and Method Metric 12: Low All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing. Domain 4: Test Animals Metric 13: Test Animal Characteristics High All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate. Metric 14: Adequacy and Consistency of Animal Medium All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was **Husbandry Conditions** not reported. Metric 15: Number of Animals per Group Medium All Outcomes: 10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.

HERO ID: 1772371 Table: 17 of 26

Comments

#### ... continued from previous page

Rating

Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health

Reproductive/Developmental; Lung/Respiratory;

Metric

Outcome(s):

Reported Health

Domain

Reproductive/Developmental: Organ weight (Testis); histopathology; Lung/Respiratory: Organ weight, histopathology;

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

	1.10.110	71441115	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Exposed and control animals were consistently observed for this outcome.
Metric 18:	Sampling Adequacy	Low	All Outcomes: Organ weights were measured for all surviving main group animals; Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.
Metric 20:	Negative Control Response	Low	Reproductive/Developmental: The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight); Lung/Respiratory: The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight).
Domain 6: Confounding / Variable Co	ntrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	All Outcomes: The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 70% decrease in water intake at the highest dose. This was reported to result in dehydration which was reflected in hematology and serum chemistry and organ weight results.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Appropriate statistical analysis was described for organ weight and histopathology
Metric 24:	Reporting of Data	Low	All Outcomes: Relevant organ weights were adequately reported. Histopathology results for this outcome were not reported.

## **Overall Quality Determination**

HERO ID: 1772371 Table: 18 of 26

1	1 - I `	)ich	loroethane

Study Citation:	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice						
Health	(drinking water and gavage studies). Gastrointestinal; Musculoskeletal; Ocular/Sensory;						
Outcome(s):	Gastrointestinal; Musculoskeletal; Octial/Sensory;  Gastrointestinal: Histopathology; Musculoskeletal: Related histology; Ocular/Sensory: Histopathology (if grossly abnormal);						
Reported Health							
Effect(s):							
Duration:	Subchronic (	(>30-91 days) 13-weeks; drinking water; rats					
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	1772371	1,2 21011101101111101					
Domain		Metric	Rating	Comments			
Domain 1: Test Substar	nce						
	Metric 1:	Test Substance Identity	High	All Outcomes: Name, sturcture and CASRN provided			
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source, analytically verified			
	Metric 3:	Test Substance Purity	High	All Outcomes: 99% purity			
			-				
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Water only control			
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type			
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers			
				table of faildoin numbers and to groups by another table of faildoin numbers			
Domain 3: Exposure C	haracterization						
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).			
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance was administered consistently across study groups			
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.			
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Continuously via drinking water for 13-weeks			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.			
	Metric 12:	Exposure Route and Method	Low	All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.			
Domain 4: Test Animal	ls						
Zoman i. 16st / millian	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.			

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		cor	ntinued from previous	page			
Study Citation:	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).  Gastrointestinal; Musculoskeletal; Ocular/Sensory;						
Health							
Outcome(s):							
Reported Health	Gastrointestinal: Histopathology; Musculoskeletal: Related histology; Ocular/Sensory: Histopathology (if grossly abnormal);						
Effect(s):							
Duration:		(>30-91 days) 13-weeks; drinking water; rats					
Chemical: HERO ID:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	1772371						
Domain		Metric	Rating	Comments			
Domain 5: Outcome	Assessment						
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.			
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.			
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.			
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological responses of the negative control group(s) were not reported.			
Domain 6: Confound	ling / Variable Co	ntrol					
Domain of Comouna	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	All Outcomes: The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 70% decrease in water intake at the highest dose. This was reported to result in dehydration which could have an impact on study results			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	Gastrointestinal: Appropriate statistical analysis was described for organ weight and histopathology; Musculoskeletal: Appropriate statistical analysis was described for organ weight and histopathology; Ocular/Sensory: Appropriate statistical analysis was described			
	Metric 24:	Reporting of Data	Uninformative	Gastrointestinal: Histopathology results for this organ/system were not reported; Musculoskeletal: Histopathology results for this organ/system were not reported; Ocular/Sensory: Histopathology results for this organ system were not reported, including no statements indicating whether no effects were observed.			

## **Overall Quality Determination**

HERO ID: 1772371 Table: 19 of 26

All Outcomes: Species, strain, sex, age, source and initial BW were reported and were

All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was

All Outcomes: 10/sex for the main group, plus an additional 10 males/sex for hematol-

Metric 13:

Metric 14:

Metric 15:

Test Animal Characteristics

Number of Animals per Group

**Husbandry Conditions** 

Adequacy and Consistency of Animal

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies). Health Renal/Kidney; Hepatic/Liver; Outcome(s): Reported Health Renal/Kidney: Organ weight; histopathology; Hepatic/Liver: Organ weight; histopathology; serum chemistry; Effect(s): **Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1772371 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High All Outcomes: Name, sturcture and CASRN provided Metric 2: Test Substance Source High All Outcomes: Commercial source, analytically verified Metric 3: Test Substance Purity High All Outcomes: 99% purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: Water only control Metric 5: Positive Controls N/A All Outcomes: Not necessary for the study type Metric 6: Medium Randomized Allocation of Animals All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers Domain 3: Exposure Characterization Preparation and Storage of Test Metric 7: High All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize Substance losses (water replaced daily). Consistency of Exposure Metric 8: High Renal/Kidney: Test substance was administered consistently across study groups.; Hepatic/Liver: Test substance was administered consistently across study groups Administration Metric 9: Reporting of Doses/Concentrations Low All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity. **Exposure Frequency and Duration** High Metric 10: All Outcomes: Continuously via drinking water for 13-weeks Metric 11: Number of Exposure Groups and High All Outcomes: 6 dose-groups including controls; doses selected were influenced by Dose/Concentration Spacing solubility being a limiting factor. Exposure Route and Method Metric 12: Low All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing. Domain 4: Test Animals

Continued on next page ...

High

Medium

Medium

appropriate.

not reported.

ogy and clinical chemistry.

HERO ID: 1772371 Table: 19 of 26

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

Health

Renal/Kidney; Hepatic/Liver;

**Outcome(s):** 

**Reported Health** 

Renal/Kidney: Organ weight; histopathology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;

Effect(s):

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

HERO ID:	1772371	retifaire- isomer. 1,2-Diemoroctifaire		
Domain		Metric	Rating	Comments
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.
	Metric 18:	Sampling Adequacy	Low	Renal/Kidney: Organ weights were measured for all surviving main group animals; Histology was done on control and high dose animals only. Hematology and clinical chemistry were performed on males only. and were performed only for the top 3 dose groups. There were inconsistencies in the number of animals evaluated/group. These differences can not be explained by deaths, and no further explanations were provided. For example, an extra set of 10 males were used for hematology and clinical chemistry. On study day 3 in F344/N rats at 2000 ppm, means for BUN were derived from only 4 animals, while 9 animals were used for creatinine kinase, and 7 for sorbitol dehydrogenase. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided. Histological examination of the kidney was apparently conducted in additional dose groups, but complete details were not provided; Hepatic/Liver: Organ weights were measured for all surviving main group animals; Histology was done on control and high dose animals only. Hematology and clinical chemistry were performed on males only. Hematology and clinical chemistry were performed only for the top 3 dose groups. There were inconsistencies in the number of animals evaluated/group. These differences can not be explained by deaths, and no further explanations were provided. For example, an extra set of 10 males were used for hematology and clinical chemistry. On study day 3 in F344/N rats at 2000 ppm, means for BUN were derived from only 4 animals, while 9 animals were used for creatinine kinase, and 7 for sorbitol dehydrogenase. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Medium	All Outcomes: Negative control-related organ weights and serum chemistry/hematology parameters were appropriate; histopathology data were selectively reported and did not include all control response details for this target/organ system.
Domain 6: Confoun	ding / Variable Co	ntrol		
20main o. Comoun	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	All Outcomes: The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 70% decrease in water intake at the highest dose. This was reported to result in dehydration which was reflected in hematology and serum chemistry and organ weight results.

Human Health Hazard Animal Toxicology Evaluation HERO ID: 1772371 Table: 19 of 26

#### ... continued from previous page

Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

**Health** Renal/Kidney; Hepatic/Liver;

Outcome(s):

Reported Health

Renal/Kidney: Organ weight; histopathology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Appropriate statistical analysis was described for organ weight and histopathology
	Metric 24:	Reporting of Data	High	Renal/Kidney: Relevant organ weights and clinical chemistry (when measured) were adequately reported. Incidence values for some histopathology observations were reported, otherwise, results were described in the text.; Hepatic/Liver: Relevant organ weights and clinical chemistry (when measured) were adequately reported. Histopathology results were indicated in the text as a negative response (i.e., no effects observed)

### **Overall Quality Determination**

HERO ID: 1772371 Table: 20 of 26 NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice **Study Citation:** (drinking water and gavage studies). Health Immune/Hematological Outcome(s): Reported Health Histopathology; hematology Effect(s): **Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 1772371 Comments Domain Metric Rating Domain 1: Test Substance Metric 1: Test Substance Identity High Name, sturcture and CASRN provided High Metric 2: Test Substance Source Commercial source, analytically verified Metric 3: **Test Substance Purity** High 99% purity Domain 2: Test Design Negative and Vehicle Controls High Metric 4: Water only control N/A Metric 5: Positive Controls Not necessary for the study type Metric 6: Randomized Allocation of Animals Medium Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers

				numbers and to groups byanother table of random numbers
Domain 3: Exposure	Characterization			
Zenimi er Zapesine	Metric 7:	Preparation and Storage of Test Substance	High	Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.

#### Domain 5: Outcome Assessment

HERO ID: 1772371 Table: 20 of 26

#### ... continued from previous page

Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies). Immune/Hematological

Health

Outcome(s):

**Reported Health** 

h Histopathology; hematology

Effect(s):
Duration:

Effect(s):

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain	Metric	Rating	Comments
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
Metric 17:	Consistency of Outcome Assessment	High	Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.
Metric 18:	Sampling Adequacy	Low	Organ weights were measured for all surviving main group animals. There were inconsistencies in the number of animals evaluated/group and that hematology and clinical chemistry were performed only for the top 3 dose groups. Hematology and clinical chemistry were performed on males only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
Metric 19:	Blinding of Assessors	Missing Conf	Not necessary for the outcome of interest.
Metric 20:	Negative Control Response	Medium	Negative control-related organ weights and serum chemistry/hematology parameters were appropriate; histopathology data were selectively reported and did not include all control response details for this target/organ system.
Domain 6: Confounding / Variable Con	ntrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 70% decrease in water intake at the highest dose. This was reported to result in dehydration which was reflected in hematology and serum chemistry and organ weight results.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	High	Appropriate statistical analysis was described for organ weight and histopathology
Metric 24:	Reporting of Data	Low	Relevant organ weights and hematology (when measured) were adequately reported. Histopathology results for this outcome were not provided.

### **Overall Quality Determination**

HERO ID: 1772371 Table: 21 of 26

NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice **Study Citation:** (drinking water and gavage studies). Health Neurological/Behavioral Outcome(s): Reported Health Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea Effect(s): **Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1772371 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Name, sturcture and CASRN provided Metric 2: Test Substance Source High Commercial source, analytically verified Metric 3: Test Substance Purity High 99% purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High Water only control N/A Metric 5: Positive Controls Not necessary for the study type Metric 6: Medium Randomized Allocation of Animals Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers Domain 3: Exposure Characterization Preparation and Storage of Test Metric 7: High Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water Substance replaced daily). Consistency of Exposure High Metric 8: Test substance was administered consistently across study groups Administration Reporting of Doses/Concentrations Metric 9: Low Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity. Metric 10: **Exposure Frequency and Duration** High Continuously via drinking water for 13-weeks Number of Exposure Groups and Metric 11: High 6 dose-groups including controls; doses selected were influenced by solubility being a Dose/Concentration Spacing limiting factor. Exposure Route and Method Metric 12: Low The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing. Domain 4: Test Animals Metric 13: Test Animal Characteristics High Species, strain, sex, age, source and initial BW were reported and were appropriate. Metric 14: Adequacy and Consistency of Animal Medium Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported. **Husbandry Conditions** Metric 15: Number of Animals per Group Medium 10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry. Domain 5: Outcome Assessment Continued on next page ...

		coi	ntinued from previous p	page		
Study Citation:	NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).					
Health	Neurological/Behavioral					
Outcome(s): Reported Health Effect(s):	Histopatholo	ogy; organ weight (brain), clinical signs includ	led tremors, salivation, ea	maciation, abnormal postures, ruffled fur, and dyspnea		
Duration:	Subchronic (	(>30-91 days) 13-weeks; drinking water; rats				
Chemical:		bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	1772371	·				
Domain		Metric	Rating	Comments		
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.		
	Metric 17:	Consistency of Outcome Assessment	High	Exposed and control animals were consistently observed for this outcome.		
	Metric 18:	Sampling Adequacy	Medium	Although it is acceptable to perform histology in only the high-dose group and control group when no effects are observed at the high dose (e.g., see OECD 409), the results of histological examination are not provided in detail for each organ, resulting in uncertainties in whether tissues/organs were affected and preventing an assessment of the appropriateness of doses selected for histopathology examinations. The number of animals evaluated for each organ is also not presented. Therefore, a full assessment of the appropriateness of the number of animals evaluated for each organ and the doses selected for histopathology cannot be made.		
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.		
	Metric 20:	Negative Control Response	Low	The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight)		
Domain 6: Confoundi	ng / Variable Co	ntrol				
Domain o. Comound	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 70% decrease in water intake at the highest dose. This was reported to result in dehydration which was reflected in hematology and serun chemistry and organ weight results.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.		
	Metric 23:	Data Presentation and Analysis	Low	Appropriate methods of statistical analyses of organ weight and histology data were used. Behavioral clinical signs data were not statistically analyzed and this data were provided for independent review.		
	Metric 24:	Reporting of Data	Low	Relevant organ weight was adequately reported. Results of clinical observations were described in the text as negative. Histopathology results for this outcome were not reported.		

HERO ID: 1772371 Table: 22 of 26

1,1-Dichloroethane

Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).

Health Renal/Kidney

**Outcome(s):** 

**Reported Health** 

Organ weight; histopathology

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 13-Week; Drinking water; mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	99% purity
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Water only control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure C	haracterization			
Domain J. Exposure C	Metric 7:	Preparation and Storage of Test	High	Details of preparation were provided. Chemical stability was evaluated; stability studies
	1120110 / 1	Substance	111811	were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure	High	Test substance was administered consistently across study groups
		Administration	-	
	Metric 9:	Reporting of Doses/Concentrations	Low	Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Animal	s			
Domain 1. 10st / illillidi	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent
	1/10/110 11.	Husbandry Conditions	1/10/10/11	between exposed and control groups. The number of animals per cage was not reported
	Metric 15:	Number of Animals per Group	Medium	10/sex/group

#### Domain 5: Outcome Assessment

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).

Health

Renal/Kidney

**Outcome(s):** 

**Reported Health** 

Organ weight; histopathology

Effect(s): Duration:

Subchronic (>30-91 days) 13-Week; Drinking water; mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain	Metric	Rating	Comments
Metric 16	: Outcome Assessment Methodology	Medium	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest. Hematology and clinical chemistry measurements were not conducted in the mouse study.
Metric 17	: Consistency of Outcome Assessment	High	Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.
Metric 18	: Sampling Adequacy	Low	Organ weights were measured for all surviving main group animals; Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
Metric 19	: Blinding of Assessors	N/A	Not necessary for the outcome of interest.
Metric 20	: Negative Control Response	High	The biological responses of the negative control group(s) were reported and were adequate
Domain 6: Confounding / Variable 0	Control		
Metric 21	: Confounding Variables in Test Design and Procedures	Low	Food intake was not reported. There was reported variation in drinking water intake from week to week during the study, and uncertainty in how intakes varied across the groups.
Metric 22	: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23	: Data Presentation and Analysis	High	Appropriate statistical analysis was described for organ weight, clincial chemistry and histopathology
Metric 24	Reporting of Data	High	Relevant organ weights were adequately reported. Incidence values for some histopathology observations were reported.

### **Overall Quality Determination**

### High

Study Citation:	NTP. (1991). Toxicity studies of 1.2-dichloroetha	thane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mic	e
Study Citation.	1111, (1991). TOXICITY STUDIES OF 1,2-dictiloroctila	mane (emplene dicinornae) in 1944/19 rats, Sprague Dawley rats, Osborne-Mender rats, and Docsi i into	C

(drinking water and gavage studies). Immune/Hematological; Hepatic/Liver; Health

**Outcome(s):** 

Reported Health Immune/Hematological: Histopathology; hematology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 13-Week; Drinking water; mice

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	All Outcomes: 99% purity
Domain 2: Test Design				
· ·	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Water only control
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups byanother table of random numbers
Domain 3: Exposure C	haracterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure Administration	High	Immune/Hematological: Test substance was administered consistently across study groups; Hepatic/Liver: Test substance was administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Animal	ls			
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported.
	Metric 15:	Number of Animals per Group	Medium	Immune/Hematological: 10/sex/group; Hepatic/Liver: 10/sex/group.

### Human Health Hazard Animal Toxicology Evaluation

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Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

**Health** Immune/Hematological; Hepatic/Liver;

**Outcome(s):** 

Reported Health

Immune/Hematological: Histopathology; hematology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;

Effect(s):

**Duration:** Subchronic (>30-91 days) 13-Week; Drinking water; mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The outcome assessment methods for this organ/system were limited because hematology and clinical chemistry measurements were not conducted in the mouse study.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.
	Metric 18:	Sampling Adequacy	Low	Immune/Hematological: Organ weights were measured for all surviving main group animals; Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided; Hepatic/Liver: Organ weights were measured for all surviving main group animals; Histology was done on control and high dose animals only. The number of animals evaluated histologically for each organ is unclear because a full presentation of histological results is not provided.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Low	Immune/Hematological: The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight).; Hepatic/Liver: The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight)
Domain 6: Confoun	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Immune/Hematological: The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight).; Hepatic/Liver: Food intake was not reported. There was reported variation in drinking water intake from week to week during the study, and uncertainty in how intakes varied across the groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Appropriate statistical analysis was described for organ weight and histopathology
	Metric 24:	Reporting of Data	Low	Immune/Hematological: Relevant organ weights were adequately reported. Histopathology results for this outcome were not provided.; Hepatic/Liver: Relevant organ weights were adequately reported. Histopathology results not reported for this organ/system.

### **Overall Quality Determination**

### Medium

HERO ID: 1772371 Table: 24 of 26

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies). Health Thyroid Outcome(s): Reported Health Related histology Effect(s): **Duration:** Subchronic (>30-91 days) 13-Week; Drinking water; mice Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 1772371 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Name, sturcture and CASRN provided Metric 2: Test Substance Source High Commercial source, analytically verified Metric 3: **Test Substance Purity** High 99% purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High Water only control Positive Controls N/A Metric 5: Not necessary for the study type Metric 6: Randomized Allocation of Animals Medium Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test High Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water Substance replaced daily). Metric 8: Consistency of Exposure High Test substance was administered consistently across study groups Administration

Metric 9:	Reporting of Doses/Concentrations	Low	Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
Metric 10:	Exposure Frequency and Duration	High	Continuously via drinking water for 13-weeks
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
Metric 12:	Exposure Route and Method	Low	The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.

Domain 4: Test Animals

Metric 13:	Test Animal Characteristics	High	Species, strain, sex, age, source and initial BW were reported and were appropriate.
Metric 14:	Adequacy and Consistency of Animal	Medium	Temp, humidity, lighting, water and food availability were reported to be consistent
	Husbandry Conditions		between exposed and control groups. The number of animals per cage was not reported.

Metric 15: Number of Animals per Group Medium 10/sex/group

Domain 5: Outcome Assessment

HERO ID: 1772371 Table: 24 of 26

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Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies).

**Health** Thyroid

**Outcome(s):** 

Reported Health

Related histology

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 13-Week; Drinking water; mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.
	Metric 18:	Sampling Adequacy	Low	Histology was done on control and high dose animals only. The number of animals eval- uated histologically for each organ is unclear because a full presentation of histological results is not provided.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Low	The biological responses of the negative control group(s) were not reported.
Domain 6: Confounding	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Food intake was not reported. There was reported variation in drinking water intake from week to week during the study, and uncertainty in how intakes varied across the groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Appropriate statistical analysis was described for organ weight and histopathology
	Metric 24:	Reporting of Data	Uninformative	Histopathology results for this organ/system were not reported

### **Overall Quality Determination**

Human Health Hazard Animal Toxicology Evaluation 1,1-Dichloroethane HERO ID: 1772371 Table: 25 of 26

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies). Skin/Connective Tissue; Endocrine;

**Outcome(s):** 

**Reported Health** 

Skin/Connective Tissue: Histology of skin; Endocrine: Histology of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.;

Effect(s):

Health

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	All Outcomes: Name, sturcture and CASRN provided
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source, analytically verified
	Metric 3:	Test Substance Purity	High	All Outcomes: 99% purity
Domain 2: Test Desig	gn			
·	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Water only control
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water replaced daily).
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Animals had access to drinking water ad libitum, however, the number o animals per cage was not reported.
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Continuously via drinking water for 13-weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: 6 dose-groups including controls; doses selected were influenced by solubility being a limiting factor.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing.
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.

# Human Health Hazard Animal Toxicology Evaluation

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Study Citation: NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice

(drinking water and gavage studies). Skin/Connective Tissue; Endocrine;

Outcome(s):

Reported Health

Skin/Connective Tissue: Histology of skin; Endocrine: Histology of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.;

**Effect(s):** 

Health

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain		Metric	Rating	Comments
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The outcome assessment methods for this organ/system were limited (histology only)
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Of the groups evaluated, exposed and control animals were consistently assessed for this outcome.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Histology was done on control and high dose animals only.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological responses of the negative control group(s) were not reported.
Domain 6: Confoun	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	All Outcomes: The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 60% decrease in water intake at the highest dose. This was reported to result in dehydration which could have an impact
				on study results
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	
	Metric 22: Metric 23:		Medium High	on study results  All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to

### **Overall Quality Determination**

HERO ID: 1772371 Table: 26 of 26

NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice **Study Citation:** (drinking water and gavage studies). Health Cardiovascular Outcome(s): Reported Health Organ weight (heart), histopathology Effect(s): **Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1772371 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Name, sturcture and CASRN provided Metric 2: Test Substance Source High Commercial source, analytically verified Metric 3: Test Substance Purity High 99% purity Domain 2: Test Design Metric 4: Negative and Vehicle Controls High Water only control N/A Metric 5: Positive Controls Not necessary for the study type Metric 6: Medium Randomized Allocation of Animals Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers Domain 3: Exposure Characterization Preparation and Storage of Test Metric 7: High Details of preparation were provided. Chemical stability was evaluated; stability studies were performed, and based on results, measures were taken to minimize losses (water Substance replaced daily). Consistency of Exposure Medium Metric 8: Animals had access to drinking water ad libitum, however, the number of animals per cage was not reported. Administration Metric 9: Reporting of Doses/Concentrations Low Target and determined concentrations were reported, however, analysis of formulations in drinking water bottles after 24hrs indicated decreases ranging from 13% to 53% of target concentrations, thus animals exposed concentrations ranged between the initial concentration and the concentration found at the end of 24 hrs leading to some ambiguity. **Exposure Frequency and Duration** High Metric 10: Continuously via drinking water for 13-weeks Metric 11: Number of Exposure Groups and High 6 dose-groups including controls; doses selected were influenced by solubility being a Dose/Concentration Spacing limiting factor. Exposure Route and Method Metric 12: Low The exposure route proved challenging due to the volatility of the test compound. There was also palatability issues overall leading to ambiguity in dosing. Domain 4: Test Animals Metric 13: Test Animal Characteristics High Species, strain, sex, age, source and initial BW were reported and were appropriate. Metric 14: Adequacy and Consistency of Animal Medium Temp, humidity, lighting, water and food availability were reported to be consistent between exposed and control groups. The number of animals per cage was not reported. **Husbandry Conditions** Metric 15: Number of Animals per Group Medium 10/sex for the main group, plus an additional 10 males/sex for hematology and clinical chemistry. Domain 5: Outcome Assessment Continued on next page ...

**Study Citation:** NTP, (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).

Health Cardiovascular

**Outcome(s):** 

Reported Health

Organ weight (heart), histopathology

**Effect(s):** 

**Duration:** Subchronic (>30-91 days) 13-weeks; drinking water; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1772371

Domain	Metric	Rating	Comments
Metri	e 16: Outcome Assessment Methodolo	ogy High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
Metri	e 17: Consistency of Outcome Assessi	ment High	Exposed and control animals were consistently observed for this outcome.
Metri	e 18: Sampling Adequacy	Low	Histology was done on control and high dose animals only. The number of animals eval- uated histologically for each organ is unclear because a full presentation of histological results is not provided.
Metri	e 19: Blinding of Assessors	N/A	Not necessary for the outcome of interest.
Metri	20: Negative Control Response	Low	The biological responses of the negative control group(s) were not reported for all related endpoints (only for related organ weight).
Domain 6: Confounding / Varia	ole Control		
Metri	c 21: Confounding Variables in Test and Procedures	Design Uninformative	The study reported a substantial decrease of water consumption with increasing dose for rats, which resulted in as much as a 70% decrease in water intake at the highest dose. This was reported to result in dehydration which was reflected in hematology and serum chemistry and organ weight results.
Metri	22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metri	23: Data Presentation and Analysis	High	Appropriate statistical analysis was described for organ weight and histopathology
Metri	24: Reporting of Data	Low	Relevant organ weights were adequately reported. Histopathology results for this outcome were not reported.

### **Overall Quality Determination**

Human Health Hazard Animal Toxicology Evaluation HERO ID: 194588 Table: 1 of 3

**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health Mortality

**Outcome(s):** 

**Reported Health** survival

Effect(s):

**Duration:** Chronic (>91 days) 2 yr (males)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric	1: Test Substance Identity	High	The test chemical was reported by name as ethylene dichloride (1,2 dichloroethane). CASRN was not reported.
Metric	2: Test Substance Source	High	The test substance source was not reported; however, it was analytically verified by the laboratory.
Metric	3: Test Substance Purity	Low	Purity of test substance was not reported.
Domain 2: Test Design			
Metric	4: Negative and Vehicle Controls	High	The study included concurrent negative controls (implied unfumigated diet) and conditions were not explicitly stated but assumed to be consistent with the treated animals.
Metric	5: Positive Controls	N/A	Positive controls are not required for this study type.
Metric	6: Randomized Allocation of Animals	Low	There were no reported details on allocation or distribution of animals.
Domain 3: Exposure Characteriza	ation		
Metric		Medium	The test substance preparation was as follows: feed was exposed to the test substance in hermetically sealed containers and stored in polyvinyl bags coated in polyamide or sealed hermetically in glass jars with a polyamide layered plastic lid. The fumigated feed was stored for a maximum storage duration of 10 days during which loss was analyzed to be approximately 5%.
Metric	8: Consistency of Exposure Administration	Medium	The test substance was administered via furnigated diet. Feed mash was administered for a limited period (1 or 2 hours) twice a day at the same time each day. Consumption and concentration of the test substance was measured in effort to maintain consistency. It was not reported whether animals were trained to the limited feeding schedule prior to implementation.
Metric	9: Reporting of Doses/Concentrations	Medium	Administered diet concentration (ppm) were reported (250 and 500 ppm). Diet was weighed (weekly) in order to determine amount consumed but those results were not reported. Feed was consumed primarily in the evening time frame with the majority during the first hour indicating the dose was consumed largely in a small time frame. Doses present in the diet after the 1-2h consumption period were reportedly 60-70% that of initially in mash and the authors stated, "since the amount eaten and the residue level were known, the amount of fumigant actually consumed was calculated with fair accuracy", therefore, it is implied that this was accounted for. It is unclear if the introduction of diet for limited time frames caused any initial changes in food consumption, thus altering the dose consumed, though the authors reported the animals "grew accustomed to consuming it quickly". It is unclear if the amount consumed is consistent to that consumed if feed were presented ad libitum. The doses could potentially be calculated.

**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

Effect(s):

survival

**Duration:** 

Chronic (>91 days) 2 yr (males)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	Low	Animals were administered the test substance in the diet twice daily for 1 hour in the day and 2 hours in the evening, for 7 days/week. This exposure frequency differs from typical study design but was altered due to test substance volatility. Exposure duration was possibly 2yr but unclear if the groups for long term study are different from those in the repro study (that were on control diet during mating).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The number of exposure groups was limited to 2 treated groups and a control. Dose spacing did not encompass any effects therefore it is unclear whether spacing was appropriate.
	Metric 12:	Exposure Route and Method	Medium	The exposure method was not suited to the test substance. The test substance is volatile, and it was prepared in the diet. However, the authors attempted to mitigate the issues of volatility in feed via sealed fumigation, limited feeding times and monitoring of the test substance residues.
Domain 4: Test Anima	ale			
Domain 4. Test Aining	Metric 13:	Test Animal Characteristics	Low	Animal characteristics were not completely reported. The details included the species (rats) and sex (male). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not sufficiently reported to evaluate adequacy.
	Metric 15:	Number of Animals per Group	Low	The number of animals (18/group) were reported and were fewer than necessary for this study type.
Domain 5: Outcome A	Assessment			
Bonain 3. Gutcome 1	Metric 16:	Outcome Assessment Methodology	Medium	Animals were observed for morbidity and mortality. The outcome assessment was sensitive and appropriate for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The outcome assessment was briefly described and was carried out consistently across groups.
	Metric 18:	Sampling Adequacy	High	All animals were sampled for the outcome of interest as reported in month 0 of table 5.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary because this outcome of interest is not subjective in nature or is not required for this outcome of interest.
	Metric 20:	Negative Control Response	Low	Negative control animals had reduced survival.

Domain 6: Confounding / Variable Control

HERO ID: 194588 Table: 1 of 3

#### ... continued from previous page

**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Mortality **Outcome(s):** 

**Reported Health** 

survival

**Effect(s):** 

**Duration:** Chronic (>91 days) 2 yr (males)

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Information to determine confounding was not reported. No differences were identified from the reported information. With the measured residue of the test substance being 60-70% in feed after the feeding period (of 1-2 hours) it is possible that due to the volatility of the test substance, some was inhaled. Information regarding food consumption was insufficient so it is unclear whether the animals consumed an amount similar to that of feed presented ad libitum. It is unclear whether there were palatability issues (if there were, they may have been complicated by the intermittent feeding).
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	It was reported that animals at 14 months and greater exhibited chronic respiratory disease- confirmed by necropsy that reduced survival. Additionally, reproduction ceased as animals aged.
	Metric 23:	Data Presentation and Analysis	Low	Statistical methods were used and reported as analysis of variance with Duncan multiple range test pairwise comparison. Significance was denoted in tables and figures. It is unclear whether this method was applied to survival, but is not an appropriate test for survival.
	Metric 24:	Reporting of Data	Medium	The study data were reported in a table for each group and discussed in the text.

### **Overall Quality Determination**

HERO ID: 194588 Table: 2 of 3

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Hepatic/Liver

**Outcome(s):** 

Reported Health

liver fat content, serum total protein, cholesterol, ALT, AST

Effect(s):

**Duration:** Chronic (>91 days) 2 yr (males)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
1	Metric 1:	Test Substance Identity	High	The test chemical was reported by name as ethylene dichloride (1,2 dichloroethane). CASRN was not reported.
I	Metric 2:	Test Substance Source	High	The test substance source was not reported; however, it was analytically verified by the laboratory.
I	Metric 3:	Test Substance Purity	Low	Purity of test substance was not reported.
Domain 2: Test Design				
2	Metric 4:	Negative and Vehicle Controls	High	The study included concurrent negative controls (implied unfumigated diet) and conditions were not explicitly stated, but assumed to be consistent with the treated animals.
1	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
I	Metric 6:	Randomized Allocation of Animals	Low	There were no reported details on allocation or distribution of animals.
Domain 3: Exposure Chara	acterization			
•	Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance preparation and storage were reported and were controlled and measured: feed was exposed to the test substance in hermetically sealed containers and stored in polyvinyl bags coated in polyamide or sealed hermetically in glass jars with a polyamide layered plastic lid. maximum storage duration was 10d during which loss was analyzed to be ~5%.
1	Metric 8:	Consistency of Exposure Administration	Medium	The test substance was administered via fumigated diet. Feed mash was administered for a limited period (1 or 2 hours) twice a day at the same time each day. Consumption and concentration of the test substance was measured in effort to maintain consistency. It was not reported whether animals were trained to the limited feeding schedule prior to implementation.
1	Metric 9:	Reporting of Doses/Concentrations	Medium	Administered diet concentration (ppm) were reported. Diet was weighed (weekly) in order to determine amount consumed but those results were not reported. Feed was consumed primarily in the evening time frame with the majority during the first hour indicating the dose was consumed largely in a small time frame. Doses present in the diet after the 1-2h consumption period were reportedly 60-70% that of initially in mash and the authors stated, "since the amount eaten and the residue level were known, the amount of fumigant actually consumed was calculated with fair accuracy", therefore, it is implied that this was accounted for. It is unclear if the introduction of diet for limited time frames caused any initial changes in food consumption, thus altering the dose consumed, though the authors reported the animals "grew accustomed to consuming it quickly". It is unclear if the amount consumed is consistent to that consumed if feed were presented ad libitum. The doses could potentially be calculated.

HERO ID: 194588 Table: 2 of 3

#### ... continued from previous page

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated furnigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

**Health** Hepatic/Liver

Outcome(s):

**Reported Health** liver fat content, serum total protein, cholesterol, ALT, AST

Effect(s):

**Duration:** Chronic (>91 days) 2 yr (males)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain	Metric	Rating	Comments
Metric 10:	Exposure Frequency and Duration	Low	Animals were administered the test substance in the diet twice daily for 1 hour in the day and 2 hours in the evening, for 7 days/week. This exposure frequency differs from typical study design but was altered due to test substance volatility. Exposure duration was possibly 2yr but unclear if the groups for long term study are different from those in the repro study (that were on control diet during mating).
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The number of exposure groups was limited to 2 treated groups and a control. Dose spacing did not encompass any effects therefore it is unclear whether spacing was appropriate.
Metric 12:	Exposure Route and Method	Medium	The exposure method was not suited to the test substance. The test substance is volatile, and it was prepared in the diet. However, the authors attempted to mitigate the issues of volatility in feed via sealed fumigation, limited feeding times and monitoring of the test substance residues.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Low	Animal characteristics were not completely reported. The details included the species (rats) and sex (male). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not sufficiently reported to evaluate adequacy.
Metric 15:	Number of Animals per Group	Low	The number of animals (18/group) were reported and were fewer than recommended, but adequate for this study type.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment included serum chemistry only. The assessment was sensitive but only partially addressed the outcome of interest.
Metric 17:	Consistency of Outcome Assessment	High	The outcome assessment was briefly described, previously cited and was carried out consistently across groups.
Metric 18:	Sampling Adequacy	Low	In table 6 it was specified that clinical chemistry results were from groups of 3-4 males, though the mortality table indicates only 2 males from the HD group survived.
Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary because this outcome of interest is not subjective in nature or is not required for this outcome of interest.
Metric 20:	Negative Control Response	High	Negative control animals responded appropriately.

Domain 6: Confounding / Variable Control

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated furnigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Hepatic/Liver

**Outcome(s):** 

Reported Health liver fat content, serum total protein, cholesterol, ALT, AST

Effect(s):

**Duration:** Chronic (>91 days) 2 yr (males)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Information to determine confounding was not reported. No differences were identified from the reported information. With the measured residue of the test substance being 60-70% in feed after the feeding period (of 1-2 hours) it is possible that due to the volatility of the test substance, some was inhaled. Information regarding food consumption was insufficient so it is unclear whether the animals consumed an amount similar to that of feed presented ad libitum. It is unclear whether there were palatability issues (if there were, they may have been complicated by the intermittent feeding).
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	It was reported that animals at 14 months and greater exhibited chronic respiratory disease- confirmed by necropsy that reduced survival. Additionally, reproduction ceased as animals aged.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were used and reported as analysis of variance with Duncan multiple range test pairwise comparison. Significance was denoted in tables and figures. This is an appropriate method of analysis for the data type.
	Metric 24:	Reporting of Data	Medium	The study data were reported in a table for each group and discussed in the text.

### **Overall Quality Determination**

HERO ID: 194588 Table: 3 of 3

1,1-Dichloroethane

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Renal/Kidney

Outcome(s): Reported Health

serum urea, uric acid, glucose

Effect(s):

**Duration:** Chronic (>91 days) 2 yr (males)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
Domain 1: Test Substanc	e			
	Metric 1:	Test Substance Identity	High	The test chemical was reported by name as ethylene dichloride (1,2 dichloroethane). CASRN was not reported.
	Metric 2:	Test Substance Source	High	The test substance source was not reported; however, it was analytically verified by the laboratory.
	Metric 3:	Test Substance Purity	Low	Purity of test substance was not reported.
Domain 2: Test Design				
20 100 2 00 gu	Metric 4:	Negative and Vehicle Controls	High	The study included concurrent negative controls (implied unfumigated diet) and conditions were not explicitly stated, but assumed to be consistent with the treated animals.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	There were no reported details on allocation or distribution of animals.
Domain 3: Exposure Cha	racterization			
1	Metric 7:	Preparation and Storage of Test Substance	Medium	The test substance preparation was as follows: feed was exposed to the test substance in hermetically sealed containers and stored in polyvinyl bags coated in polyamide or sealed hermetically in glass jars with a polyamide layered plastic lid. The fumigated feed was stored for a maximum storage duration of 10 days during which loss was analyzed to be approximately 5%.
	Metric 8:	Consistency of Exposure Administration	Medium	The test substance was administered via fumigated diet. Feed mash was administered for a limited period (1 or 2 hours) twice a day at the same time each day. Consumption and concentration of the test substance was measured in effort to maintain consistency. It was not reported whether animals were trained to the limited feeding schedule prior to implementation.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Administered diet concentration (ppm) were reported. Diet was weighed (weekly) in order to determine amount consumed but those results were not reported. Feed was consumed primarily in the evening time frame with the majority during the first hour indicating the dose was consumed largely in a small time frame. Doses present in the diet after the 1-2h consumption period were reportedly 60-70% that of initially in mash and the authors stated, "since the amount eaten and the residue level were known, the amount of fumigant actually consumed was calculated with fair accuracy", therefore, it is implied that this was accounted for. It is unclear if the introduction of diet for limited time frames caused any initial changes in food consumption, thus altering the dose consumed, though the authors reported the animals "grew accustomed to consuming it quickly". It is unclear if the amount consumed is consistent to that consumed if feed were presented ad libitum. The doses could potentially be calculated.

1,1-Dichloroethane

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HERO ID: 194588 Table: 3 of 3

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated furnigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Renal/Kidney

**Outcome(s):** 

**Reported Health** 

serum urea, uric acid, glucose

**Effect(s):** 

**Duration:** Chronic (>91 days) 2 yr (males)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	Low	Animals were administered the test substance in the diet twice daily for 1 hour in the day and 2 hours in the evening, for 7 days/week. This exposure frequency differs from typical study design but was altered due to test substance volatility. Exposure duration was possibly 2yr but unclear if the groups for long term study are different from those in the repro study (that were on control diet during mating).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The number of exposure groups was limited to 2 treated groups and a control. Dose spacing did not encompass any effects therefore it is unclear whether spacing was appropriate.
	Metric 12:	Exposure Route and Method	Medium	The exposure method was not suited to the test substance. The test substance is volatile, and it was prepared in the diet. However, the authors attempted to mitigate the issues of volatility in feed via sealed fumigation, limited feeding times and monitoring of the test substance residues.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	Animal characteristics were not completely reported. The details included the species (rats) and sex (male and female). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not sufficiently reported to evaluate adequacy.
	Metric 15:	Number of Animals per Group	Low	The number of animals (18/group) were reported and were fewer than recommended, but adequate for this study type.
Domain 5: Outcome Asse	essment			
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment included serum chemistry only. The assessment was sensitive but only partially addressed the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The outcome assessment was briefly described, previously cited and was carried out consistently across groups.
	Metric 18:	Sampling Adequacy	Low	In table 6 it was specified that clinical chemistry results were from groups of 3-4 males, though the mortality table indicates only 2 males from the HD group survived.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary because this outcome of interest is not subjective in nature or is not required for this outcome of interest.
	Metric 20:	Negative Control Response	Medium	Negative control animals responded appropriately.

Domain 6: Confounding / Variable Control

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Renal/Kidney

Outcome(s): Reported Health

serum urea, uric acid, glucose

**Effect(s):** 

**Duration:** Chronic (>91 days) 2 yr (males)

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Information to determine confounding was not reported. No differences were identified from the reported information. With the measured residue of the test substance being 60-70% in feed after the feeding period (of 1-2 hours) it is possible that due to the volatility of the test substance, some was inhaled. Information regarding food consumption was insufficient so it is unclear whether the animals consumed an amount similar to that of feed presented ad libitum. It is unclear whether there were palatability issues (if there were, they may have been complicated by the intermittent feeding).
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	It was reported that animals at 14 months and greater exhibited chronic respiratory disease- confirmed by necropsy that reduced survival. Additionally, reproduction ceased as animals aged.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were used and reported as analysis of variance with Duncan multiple range test. Significance was denoted in tables and figures. This is an appropriate method of analysis for the data type.
	Metric 24:	Reporting of Data	Medium	The study data were reported in a table for each group and discussed in the text.

### **Overall Quality Determination**

**Study Citation:** 

Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.

HERO ID: 12097 Table: 1 of 3

Health
Outcome(s):
Reported Health
Effect(s):

Cancer/Carcinogenesis; Nutritional/Metabolic; Thyroid; Neurological/Behavioral; Cardiovascular; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Mortality; Renal/Kidney; Ocular/Sensory; Lung/Respiratory; Skin/Connective Tissue;

Cancer/Carcinogenesis: Incidence of observed tumors was reported; Nutritional/Metabolic: Body weight and food and water consumption; Thyroid: Examine and histology on thyroid; Neurological/Behavioral: Examined brain, sciatic nerve, spinal cordHistology on brain; Cardiovascular: Examined: aorta, heartHistology: heart; Gastrointestinal: Examine: esophagus, large intestine, salivary glands, stomach, small intestineHistology: colon, esophagus, small intestine, stomach, salivary gland; Immune/Hematological: Examine: lymph nodes (thoracic and mesenteric), bone marrow, thymus, spleenHistology: lymph nodes (thoracic and mesenteric), bone marrow, spleen, thymus; Hepatic/Liver: liver weight, gross pathology and histology, and liver covalent DNA binding; Musculoskeletal: Examine: skeletal muscle, sternum, vertebral bone, skullHistology: bone, bone marrow, subcutis; Mortality: Mortality; Renal/Kidney: Examine: kidney, urinary bladderHistology: kidney, urinary bladder; Renal/Kidney: Examine: kidney, urinary bladderHistology: kidney, urinary bladder; Ocular/Sensory: Examine: eyes; Lung/Respiratory: Examine: lungs, trachea, larnyx and pharynx, nasal cavity and turbinatesHistology: larynx, lung, nasal cavity/mucus membrane, trachea; Skin/Connective Tissue: Examine: adipose tissue, skinHistology: skin;

**Duration:** Chronic (>91 days) 2 year

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 12097

Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Cancer/Carcinogenesis: Test substance was identified as ethylene dichloride (1,2dichloroethane) with CASRN 107-06-2.; Nutritional/Metabolic: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Thyroid: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Neurological/Behavioral: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Cardiovascular: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Gastrointestinal: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Immune/Hematological: Test substance was identified as ethylene dichloride (1,2dichloroethane).; Hepatic/Liver: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Musculoskeletal: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Mortality: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Renal/Kidney: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Renal/Kidney: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Ocular/Sensory: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Lung/Respiratory: Test substance was identified as ethylene dichloride (1,2-dichloroethane).; Skin/Connective Tissue: Test substance was identified as ethylene dichloride (1,2-dichloroethane).

### Human Health Hazard Animal Toxicology Evaluation

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**Study Citation:** 

Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.

Health
Outcome(s):
Reported Health
Effect(s):

Cancer/Carcinogenesis; Nutritional/Metabolic; Thyroid; Neurological/Behavioral; Cardiovascular; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Mortality; Renal/Kidney; Ocular/Sensory; Lung/Respiratory; Skin/Connective Tissue;

Cancer/Carcinogenesis; Incidence of observed tumors was reported; Nutritional/Metabolic; Body weight and food and water consumption; Thyroid; Example 1997 (1997) (

Cancer/Carcinogenesis: Incidence of observed tumors was reported; Nutritional/Metabolic: Body weight and food and water consumption; Thyroid: Examine and histology on thyroid; Neurological/Behavioral: Examined brain, sciatic nerve, spinal cordHistology on brain; Cardiovascular: Examined: aorta, heartHistology: heart; Gastrointestinal: Examine: esophagus, large intestine, salivary glands, stomach, small intestineHistology: colon, esophagus, small intestine, stomach, salivary gland; Immune/Hematological: Examine: lymph nodes (thoracic and mesenteric), bone marrow, thymus, spleenHistology: lymph nodes (thoracic and mesenteric), bone marrow, spleen, thymus; Hepatic/Liver: liver weight, gross pathology and histology, and liver covalent DNA binding; Musculoskeletal: Examine: skeletal muscle, sternum, vertebral bone, skullHistology: bone, bone marrow, subcutis; Mortality; Renal/Kidney: Examine: kidney, urinary bladderHistology: kidney, urinary bladder; Ocular/Sensory: Examine: eyes; Lung/Respiratory: Examine: lungs, trachea, larnyx and pharynx, nasal cavity and turbinatesHistology: larynx, lung, nasal cavity/mucus membrane, trachea; Skin/Connective Tissue: Examine: adipose tissue, skinHistology: skin;

Duration: Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Chronic (>91 days) 2 year

**HERO ID:** 12097

Domain Metric Rating Comments

Metric 2: Test Substance Source High

Cancer/Carcinogenesis: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. Batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Nutritional/Metabolic: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported but the test substance was analytically verified by the laboratory.; Thyroid: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Neurological/Behavioral: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Cardiovascular: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Gastrointestinal: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Immune/Hematological: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Hepatic/Liver: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Musculoskeletal: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Mortality: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Renal/Kidney: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Renal/Kidney: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Ocular/Sensory: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Lung/Respiratory: The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch or lot number was not reported, but the test substance was analytically verified by the laboratory.; Skin/Connective Tissue: The source of the test substance was Aldrich Chemical Co. Milwaukee, WI. The batch or lot number was not reported, but the test substance was

Page **676** of **955**lytically verified by the laboratory.

**Study Citation:** 

### ... continued from previous page

oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.

Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on

Health Outcome(s): Reported Health Effect(s):  Duration: Chemical: HERO ID:	atic/Liver; M Cancer/Carc amine and hi heartHistolog intestine, sto lymph nodes DNA binding Renal/Kidne urinary bladd larynx, lung, Chronic (>9	Jusculoskeletal; Mortality; Renal/Kidney; inogenesis: Incidence of observed tumors stology on thyroid; Neurological/Behavio gy: heart; Gastrointestinal: Examine: esogmach, salivary gland; Immune/Hematolog; (thoracic and mesenteric), bone marrow g; Musculoskeletal: Examine: skeletal my: Examine: kidney, urinary bladderHistoler; Ocular/Sensory: Examine: eyes; Lun	Renal/Kidney was reported ral: Examine phagus, large gical: Exami v, spleen, thy uscle, sternur blogy: kidney g/Respiratory	ogical/Behavioral; Cardiovascular; Gastrointestinal; Immune/Hematological; Hep- y; Ocular/Sensory; Lung/Respiratory; Skin/Connective Tissue; I; Nutritional/Metabolic: Body weight and food and water consumption; Thyroid: Ex- d brain, sciatic nerve, spinal cordHistology on brain; Cardiovascular: Examined: aorta, intestine, salivary glands, stomach, small intestineHistology: colon, esophagus, small ine: lymph nodes (thoracic and mesenteric), bone marrow, thymus, spleenHistology: mus; Hepatic/Liver: liver weight, gross pathology and histology, and liver covalent n, vertebral bone, skullHistology: bone, bone marrow, subcutis; Mortality: Mortality; n, urinary bladder; Renal/Kidney: Examine: kidney, urinary bladderHistology: kidney, Examine: lungs, trachea, larnyx and pharynx, nasal cavity and turbinatesHistology: ve Tissue: Examine: adipose tissue, skinHistology: skin;
Domain		Metric	Rating	Comments
	Metric 3:	Test Substance Purity	High	Cancer/Carcinogenesis: Purity of test substance was reported as >99% and purity was verified by HPLC.; Nutritional/Metabolic: Purity of test substance was reported as >99%.; Thyroid: Purity of test substance was reported as >99%.; Neurological/Behavioral: Purity of test substance was reported as >99%.; Cardiovascular: Purity of test substance was reported as >99%.; Immune/Hematological: Purity of test substance was reported as >99%.; Hepatic/Liver: Purity of test substance was reported as >99%.; Musculoskeletal: Purity of test substance was reported as >99%.; Renal/Kidney: Purity of test substance was reported as >99%.; Renal/Kidney: Purity of test substance was reported as >99%.; Renal/Kidney: Purity of test substance was reported as >99%.; Ocular/Sensory: Purity of test substance was reported as >99%.; Lung/Respiratory: Purity of test substance was reported as >99%.; Skin/Connective Tissue: Purity of test substance was reported as >99%.; Skin/Connective Tissue: Purity of test substance was reported as >99%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A negative control group was sham treated.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Study does not report how animals were allocated.
Domain 3: Exposure Ch	naracterization			
		Cont	tinued on nex	xt page

**Study Citation:** 

Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.

Health
Outcome(s):
Reported Health
Effect(s):

Cancer/Carcinogenesis; Nutritional/Metabolic; Thyroid; Neurological/Behavioral; Cardiovascular; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Mortality; Renal/Kidney; Renal/Kidney; Ocular/Sensory; Lung/Respiratory; Skin/Connective Tissue; Cancer/Carcinogenesis: Incidence of observed tumors was reported; Nutritional/Metabolic: Body weight and food and water consumption; Thyroid: Examine and histology on thyroid; Neurological/Behavioral: Examined brain, sciatic nerve, spinal cordHistology on brain; Cardiovascular: Examined: aorta, heartHistology: heart; Gastrointestinal: Examine: esophagus, large intestine, salivary glands, stomach, small intestineHistology: colon, esophagus, small intestine, stomach, salivary gland; Immune/Hematological: Examine: lymph nodes (thoracic and mesenteric), bone marrow, thymus, spleenHistology: lymph nodes (thoracic and mesenteric), bone marrow, spleen, thymus; Hepatic/Liver: liver weight, gross pathology and histology, and liver covalent DNA binding; Musculoskeletal: Examine: skeletal muscle, sternum, vertebral bone, skullHistology: bone, bone marrow, subcutis; Mortality; Mortality;

Renal/Kidney: Examine: kidney, urinary bladderHistology: kidney, urinary bladder; Renal/Kidney: Examine: kidney, urinary bladderHistology: kidney,

urinary bladder; Ocular/Sensory: Examine: eyes; Lung/Respiratory: Examine: lungs, trachea, larnyx and pharynx, nasal cavity and turbinatesHistology: larynx, lung, nasal cavity/mucus membrane, trachea; Skin/Connective Tissue: Examine: adipose tissue, skinHistology: skin;

Rating

Duration: Chemical: Chronic (>91 days) 2 year 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 120

Domain

12097

Metric 7: Preparation and Storage of Test

Substance

Metric

Medium Cancer/Carcinogenesis: Preparation of test substance was not completely described

but the authors analytically confirmation air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization; Nutritional/Metabolic: Preparation of the test substance was not completely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization.; Thyroid: Preparation of the test substance was not completely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization.; Neurological/Behavioral: Preparation of the test substance was not completely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization.; Cardiovascular: Preparation of the test substance was not completely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization.; Gastrointestinal: Preparation of the test substance was not completely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization.; Immune/Hematological: Preparation of the test substance was not completely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization.; Hepatic/Liver: Preparation of the test substance was not completely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization.; Musculoskeletal: Preparation of the test substance was not completely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained

Comments

test substance during volatilization.; Mortality: Preparation of the test substance was not Page 678 of 955 pletely described but authors analytically confirmed air concentrations hourly. Study authors concluded that concentrations were maintained within 2% of nominal concentrations.

within 2% of nominal concentrations, indicating minimal loss or decomposition of the

		contin	ued from p	previous page			
Study Citation:				/eisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on			
Health		oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.  Cancer/Carcinogenesis; Nutritional/Metabolic; Thyroid; Neurological/Behavioral; Cardiovascular; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Mortality; Renal/Kidney; Renal/Kidney; Ocular/Sensory; Lung/Respiratory; Skin/Connective Tissue;					
Outcome(s):							
Reported Health	ed Health Cancer/Carcinogenesis: Incidence of observed tumors was reported; Nutritional/Metabolic: Body weight and food and water consumption; Thyroid						
Effect(s):							
Duration:		, nasai cavity/mucus memorane, tracnea, sk 91 days) 2 year	iii/Connecu	ve Tissue: Examine: adipose tissue, skinHistology: skin;			
Chemical:		pethane- Isomer: 1,2-Dichloroethane					
HERO ID:	12097	Schlane- Isomer. 1,2-Bemoroculane					
Domain		Metric	Rating	Comments			
	Metric 8:	Consistency of Exposure	High	All Outcomes: Test substance was delivered consistently across study groups.			
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Measured concentration and target were reported. Concentrations were within 2% of nominal concentration.			
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were reported and appropriate for this study type (7hr/day, 5 day/week for 2 years)			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	All Outcomes: Only one concentration was studied, this was based off the current US occupational standard.			
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Dynamic whole body was used with 12 air changes/hr.			
Domain 4: Test Anim	als						
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Animal characteristics were adequately described.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Husbandry conditions were adequately reported.			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was acceptable (50/sex/group).			
Domain 5: Outcome A	Assessment						
Domain 3. Sucome?	Metric 16:	Outcome Assessment Methodology	High	Cancer/Carcinogenesis: The outcome assessment methodology was appropriate.; Nutritional/Metabolic: The outcome assessment methodology appropriate.; Neurological/Behavioral: The outcome assessment methodology appropriate.; Cardiovascular: The outcome assessment methodology appropriate.; Cardiovascular: The outcome assessment methodology appropriate.; Immune/Hematological: The outcome assessment methodology appropriate.; Hepatic/Liver: The outcome assessment methodology appropriate.; The outcome assessment methodology appropriate.; Mortality: The outcome assessment methodology appropriate.; Renal/Kidney: The outcome assessment methodology appropriate.; Ocular/Sensory: The outcome assessment methodology appropriate.; Cocular/Sensory: The outcome assessment methodology appropriate.; Cocular/Sensory: The outcome assessment methodology appropriate.; Skin/Connective Tissue: The outcome assessment methodology appropriate.			
		Conti	nued on nex	** ** *			
		Contri	naca on nez	7. hu2			

Study Citation:	Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261				
Health Outcome(s): Reported Health Effect(s):  Duration: Chemical:	oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261. Cancer/Carcinogenesis; Nutritional/Metabolic; Thyroid; Neurological/Behavioral; Cardiovascular; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Mortality; Renal/Kidney; Renal/Kidney; Ocular/Sensory; Lung/Respiratory; Skin/Connective Tissue; Cancer/Carcinogenesis: Incidence of observed tumors was reported; Nutritional/Metabolic: Body weight and food and water consumption; Thyroid: Examine and histology on thyroid; Neurological/Behavioral: Examined brain, sciatic nerve, spinal cordHistology on brain; Cardiovascular: Examined: aort heartHistology: heart; Gastrointestinal: Examine: esophagus, large intestine, salivary glands, stomach, small intestineHistology: colon, esophagus, sma intestine, stomach, salivary gland; Immune/Hematological: Examine: lymph nodes (thoracic and mesenteric), bone marrow, thymus, spleenHistology lymph nodes (thoracic and mesenteric), bone marrow, spleen, thymus; Hepatic/Liver: liver weight, gross pathology and histology, and liver covaler DNA binding; Musculoskeletal: Examine: skeletal muscle, sternum, vertebral bone, skullHistology: bone, bone marrow, subcutis; Mortality: Mortality: Renal/Kidney: Examine: kidney, urinary bladderHistology: kidney urinary bladder; Renal/Kidney: Examine: kidney, urinary bladderHistology: kidney urinary bladder; Ocular/Sensory: Examine: eyes; Lung/Respiratory: Examine: lungs, trachea, larnyx and pharynx, nasal cavity and turbinatesHistology larynx, lung, nasal cavity/mucus membrane, trachea; Skin/Connective Tissue: Examine: adipose tissue, skinHistology: skin; Chronic (>91 days) 2 year 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:  Domain	12097	Metric	Rating	Comments	
Domani	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The outcomes were assessed consistently across study groups.	
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling of outcomes was adequate.	
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not applicable.	
	Metric 20:	Negative Control Response	High	Cancer/Carcinogenesis: Responses in the negative control group were appropriate.; Nutritional/Metabolic: A negative control group was adequate.; Thyroid: A negative control group was adequate.; Neurological/Behavioral: A negative control group was adequate.; Gastrointestinal: A negative control group was adequate.; Immune/Hematological: A negative control group was adequate.; Hepatic/Liver: A negative control group was adequate.; Musculoskeletal: A negative control group was adequate.; Mortality: A negative control group was adequate.; Renal/Kidney: A negative control group was adequate.; Renal/Kidney: A negative control group was adequate.; A negative control group was adequate.; Lung/Respiratory: A negative control group was adequate.; Skin/Connective Tissue: A negative control group was adequate.	
Domain 6: Confoundin	g / Variable Cor	ntrol			
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is respiratory irritant and respiratory rates were not reported.	
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.	
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was adequately reported.	
	Metric 24:	Reporting of Data	High	All Outcomes: Exposure related findings were reported adequately.	
Overall Quali	ty Dotorn	nination	High		

<b>Study Citation:</b>	Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on
	oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.

Health

Endocrine

Outcome(s): Reported Health

Examine: adrenal glands, pancreas, parathyroid, pituitaryHistology: adrenal glands, parathyroid, pituitary, pancreas

Effect(s):
Duration:

Chronic (>91 days) 2 year

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 12097

Domain		Metric	Rating	Comments
Domain 1: Test Substar	ice			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (1,2-dichloroethane).
	Metric 2:	Test Substance Source	High	The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch
				or lot number was not reported, but the test substance was analytically verified by the
	3.5	m . a	*** 1	laboratory.
	Metric 3:	Test Substance Purity	High	Purity of test substance was reported as >99%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	A negative control group was sham treated.
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
Domain 3: Exposure Cl	naracterization			
	Metric 7:	Preparation and Storage of Test	Medium	Preparation of the test substance was not completely described but authors analytically
		Substance		confirmed air concentrations hourly. Study authors concluded that concentrations were
				maintained within 2% of nominal concentrations, indicating minimal loss or decomposi-
				tion of the test substance during volatilization.
	Metric 8:	Consistency of Exposure	High	Test substance was delivered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	Uiah	Massayand concentration and toward warm remarked. Concentrations were within 20% of
	Metric 9.	Reporting of Doses/Concentrations	High	Measured concentration and target were reported. Concentrations were within 2% of nominal concentration.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate for this study type
			8	(7hr/day, 5 day/week for 2 years)
	Metric 11:	Number of Exposure Groups and	N/A	Only one concentration was studied, this was based off the current US occupational
		Dose/Concentration Spacing		standard.
	Metric 12:	Exposure Route and Method	Medium	Dynamic whole body was used with 12 air changes/hr.
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	High	Animal characteristics were adequately described.
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.
		Husbandry Conditions	8	
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was acceptable (50/sex/group).
		* *		
Domain 5: Outcome As				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	The outcomes were assessed consistently across study groups.

# Human Health Hazard Animal Toxicology Evaluation

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continued from	nrevious nage
··· communaca mom	previous page

**Study Citation:** Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261. Endocrine

Health

**Outcome(s):** 

**Reported Health** 

Examine: adrenal glands, pancreas, parathyroid, pituitaryHistology: adrenal glands, parathyroid, pituitary, pancreas

Effect(s):

Chronic (>91 days) 2 year **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 12097

Domain	Metric	Rating	Comments
Metric	18: Sampling Adequacy	High	Sampling of outcomes was adequate.
Metric	19: Blinding of Assessors	N/A	Not applicable.
Metric	20: Negative Control Response	High	A negative control group was adequate.
Domain 6: Confounding / Variab Metric	21: Confounding Variables in Test Design	Low	Test substance is respiratory irritant and respiratory rates were not reported.
0		Low	Test substance is respiratory irritant and respiratory rates were not reported.
Metric		Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric	23: Data Presentation and Analysis	High	Statistical analysis was adequately reported.
Metric	24. Reporting of Data	Medium	Incidence data for pancreas lesions were not reported

#### **Overall Quality Determination** High

Study Citation:	Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on
	oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.

Health

Reproductive/Developmental

**Outcome(s):** 

Reported Health

Examine: accessory sex organs, mammary tissue, ovaries, testes, uterus, seminal vesiclesHistology: mammary gland, ovary, prostate, testes, uterus

Effect(s):
Duration:

Chronic (>91 days) 2 year

Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 12097

Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (1,2-dichloroethane).
	Metric 2:	Test Substance Source	High	The source of the test substance was Aldrich Chemical Co, Milwaukee, WI. The batch
				or lot number was not reported, but the test substance was analytically verified by the
	Metric 3:	Test Substance Purity	High	laboratory.  Purity of test substance was reported as >99%.
	Metric 3.	Test Substance Furity	nigii	Purity of test substance was reported as >99%.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	A negative control group was sham treated.
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
Domain 3: Exposure Ch	aracterization			
Domain 5. Exposure en	Metric 7:	Preparation and Storage of Test	Medium	Preparation of the test substance was not completely described but authors analytically
		Substance		confirmed air concentrations hourly. Study authors concluded that concentrations were
				maintained within 2% of nominal concentrations, indicating minimal loss or decomposi-
				tion of the test substance during volatilization.
	Metric 8:	Consistency of Exposure	High	Test substance was delivered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	Uich	Massayrad concentration and towart ware namented. Concentrations were within 20% of
	Metric 9.	Reporting of Doses/Concentrations	High	Measured concentration and target were reported. Concentrations were within 2% of nominal concentration.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate for this study type
		1	8	(7hr/day, 5 day/week for 2 years)
	Metric 11:	Number of Exposure Groups and	N/A	Only one concentration was studied, this was based off the current US occupational
		Dose/Concentration Spacing		standard.
	Metric 12:	Exposure Route and Method	Medium	Dynamic whole body was used with 12 air changes/hr.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	High	Animal characteristics were adequately described.
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were adequately reported.
		Husbandry Conditions	Ü	
_	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was acceptable (50/sex/group).
Domain 5: Outcome As	sessment			
2 omain 5. Gutcome 715	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	The outcomes were assessed consistently across study groups.
	1.10.110 17.	·	nued on nex	, , , ,

HERO ID: 12097 Table: 3 of 3

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<b>Study Citation:</b>		Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., Weisburger, E.K. (1990). Ethylene dichloride: the influence of disulfiram or ethanol on					
Health		oncogenicity, metabolism, and DNA covalent binding in rats. Toxicological Sciences 14(2):243-261.					
Outcome(s):	Reproductive	Reproductive/Developmental					
Reported Health	Evamina: ac	cassary say argans mammary tissua avarie	ac tactac uta	erus, seminal vesiclesHistology: mammary gland, ovary, prostate, testes, uterus			
Effect(s):	Examine. ac	cessory sex organs, mammary tissue, ovarie	es, testes, ut	erus, seminai vesiciesi fistology. mainmary giand, ovary, prostate, testes, uterus			
<b>Duration:</b>	Chronic (>9	1 days) 2 year					
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	12097	•					
Domain		Metric	Rating	Comments			
	Metric 18:	Sampling Adequacy	High	Sampling of outcomes was adequate.			
	Metric 19:	Blinding of Assessors	N/A	Not applicable.			
	Metric 20:	Negative Control Response	High	A negative control group was adequate.			
Domain 6: Confound	ing / Variable Co	ntrol					
Domain of Comound	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is respiratory irritant and respiratory rates were not reported.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.			
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was not performed on gross petrological findings.			
	Metric 24:	Reporting of Data	Medium	Incidence data on testicular lesions were not reported.			
OII OI	Ľ4 D . 4		TT! _1.				
<b>Overall Qual</b>	lity Detern	nination	High				

HERO ID: 94473 Table: 1 of 2

**Study Citation:** 

Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic

and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

Survival

Effect(s):

**Duration:** Chronic (>91 days) Chronic; 3x weekly Dermal Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:

94473

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Identified as 1,2-Dichloroethane; CASRN not provided; Structure (SMILES) reported.
Metric 2:	Test Substance Source	High	Test substance was obtained from a commercial source; the batch and lot number were not provided, Identity was independently verified by the laboratory performing the experiment (NMR)
Metric 3:	Test Substance Purity	Medium	The commercial-grade of the test substance was not reported. The laboratory conducted NMR analysis to confirm the identity and purity of the test substance. The text indicates that in some cases gas chromatograms were also done to substantiate the structure. The text generally states that these methods showed no marked impurities, but specific purities of each compound evaluated were not reported.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	Low	Vehicle-only (acetone) and untreated control groups were included. The volume of the acetone control was (0.1mL) was not equal to the volume used in the treatment groups (0.2mL)
Metric 5:	Positive Controls	Medium	The study indicates a positive control was used, and reports mean survival time for this group, it does not specify what the positive control is.
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure Characterization	1		
Metric 7:	Preparation and Storage of Test Substance	Low	Preparation (in acetone) was minimally described, however no details on storage, or when preparations were made were not provided. Due to the volatility of the test substance, this could have a significant impact on results.
Metric 8:	Consistency of Exposure Administration	Low	Minimal details were provided. It is not explicitly stated whether control and experimen- tal groups were handled consistently
Metric 9:	Reporting of Doses/Concentrations	Low	The doses were reported in mg/application/mouse. No information on animal body weights was provided.
Metric 10:	Exposure Frequency and Duration	Medium	The test substance was administered 3x weekly which is not uncommon for a dermal cancer study. The for a group of chemicals, the study duration was reported to be 440-594 days, but durations for individual chemicals is not reported.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Justification for doses was not provided, but the incidence of tumors was significant at the high dose level (which was the main focus of the study).

### ... continued from previous page

**Study Citation:** Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic

and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

Mortality Health

**Outcome(s):** 

Reported Health Survival

Effect(s):

**Duration:** Chemical:

Chronic (>91 days) Chronic; 3x weekly Dermal 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94473

HERO ID.	,,			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Uninformative	The Dermal route of exposure is acceptable for the study type, however, the method of exposure did not take into account the volatility of the test substance. Based on the information provided. The test substance (in acetone) was pipetted onto clipped skin. The methods provide no indications suggesting the use of a Finn chamber or occlusive conditions to prevent evaporation. This is considered to be unacceptable for a volatile compound, especially since treatment was performed in a ventilated hood.
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Low	Animal species, strain, source, sex, and age were reported. Starting body weights were not included. Only a single-sex (females) was used for the experimental group without justification.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions were reported. Light-dark cycles were not included.
	Metric 15:	Number of Animals per Group	Low	The study reports the use of 30 animals females in the treatment group, 30 in the vehicle-only group, and 100 animals in the no-treatment group. 30 animals is lower than the number of animals recommended for a chronic carcinogenicity study.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Survival of all animals was recorded.
	Metric 17:	Consistency of Outcome Assessment	Low	It is unclear if all animals were consistently observed for a lifetime, or if surviving animals were sacrificed after equivalent exposure durations, Consistency between exposure groups and the controls is not clearly stated.
	Metric 18:	Sampling Adequacy	High	All animals were monitored for mortality
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology review.
	Metric 20:	Negative Control Response	High	The text reported that "survival of all animals was excellent"
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	The study did not report information to determine confounding
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Uninformative	Statistical analysis was not performed. Data were not provided for independent review.
	Metric 24:	Reporting of Data	Uninformative	Survival data for individual chemicals were not reported.

# **Overall Quality Determination**

### Uninformative

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

HERO ID: 94473 Table: 1 of 2

### ... continued from previous page

Study Citation: Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic

and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

**Health** Mortality

**Outcome(s):** 

**Reported Health** Survival

Effect(s):

**Duration:** Chronic (>91 days) Chronic; 3x weekly Dermal **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94473

Domain Metric Rating Comments

Study Citation: Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic

and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

Health Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** Tumor initiation assay: Skin, lung, stomach tumors

**Effect(s):** 

**Duration:** Chronic (>91 days) Chronic; 3x weekly Dermal **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94473

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Identified as 1,2-Dichloroethane; CASRN not provided; Structure (SMILES) reported.
Metric 2:	Test Substance Source	High	Test substance was obtained from a commercial source; the batch and lot number were not provided, Identity was independently verified by the laboratory performing the experiment (NMR)
Metric 3:	Test Substance Purity	Medium	The commercial-grade of the test substance was not reported. The laboratory conducted NMR analysis to confirm the identity and purity of the test substance. The text indicates that in some cases gas chromatograms were also done to substantiate the structure. The text generally states that these methods showed no marked impurities, but specific purities of each compound evaluated were not reported.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	Low	Vehicle-only (acetone) and untreated control groups were included. The volume of the acetone control was (0.1mL) was not equal to the volume used in the treatment groups (0.2mL)
Metric 5:	Positive Controls	Medium	The study indicates a positive control was used, and reports mean survival time for this group, it does not specify what the positive control is.
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure Characterizati	on		
Metric 7:		Low	Preparation (in acetone) was minimally described, however no details on storage, or when preparations were made were not provided. Due to the volatility of the test substance, this could have a significant impact on results.
Metric 8:	Consistency of Exposure Administration	Low	Minimal details were provided. It is not explicitly stated whether control and experimental groups were handled consistently
Metric 9:		Low	The doses were reported in mg/application/mouse. No information on animal body weights was provided.
Metric 10	Exposure Frequency and Duration	Medium	The test substance was administered 3x weekly which is not uncommon for a dermal cancer study. The for a group of chemicals, the study duration was reported to be 440-594 days, but durations for individual chemicals is not reported.
Metric 1	: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Justification for doses was not provided, but the incidence of tumors was significant at the high dose level.

Study Citation: Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

Health

Cancer/Carcinogenesis

Outcome(s): Reported Health

Tumor initiation assay: Skin, lung, stomach tumors

**Effect(s):** 

**Duration:** Chronic (>91 days) Chronic; 3x weekly Dermal **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94473

Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Uninformative	The Dermal route of exposure is acceptable for the study type, however, the method of exposure did not take into account the volatility of the test substance. Based on the information provided. The test substance (in acetone) was pipetted onto clipped skin. The methods provide no indications suggesting the use of a Finn chamber or occlusive conditions to prevent evaporation. This is considered to be unacceptable for a volatile compound, especially since treatment was performed in a ventilated hood.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Low	Animal species, strain, source, sex, and age were reported. Starting body weights were not included. Only a single-sex (females) was used for the experimental group without justification.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions were reported. Light-dark cycles were not included.
	Metric 15:	Number of Animals per Group	Low	The study reports the use of 30 animals females in the treatment group, 30 in the vehicle-only group, and 100 animals in the no-treatment group. 30 animals is lower than the number of animals recommended for a chronic carcinogenicity study.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Criteria for outcome assessment (tumor incidence) was minimally described. Some additional details were available in a cited reference.
	Metric 17:	Consistency of Outcome Assessment	Low	It is unclear if all animals were consistently observed for a lifetime, or if surviving animals were sacrificed after equivalent exposure durations, Consistency between exposur groups and the controls is not clearly stated.
	Metric 18:	Sampling Adequacy	High	All animals were monitored for development of tumors
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology review.
	Metric 20:	Negative Control Response	High	The text did not indicate concern about tumor incidences in the negative control group
Domain 6: Confoundin	g / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	The study did not report information to determine confounding
	Metric 22:	and Procedures Health Outcomes Unrelated to	Medium	There was no information either to support or dismiss the suggestion that there were
		Exposure		differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was included and appropriate for the outcome of interest; however, the control group used for comparison (vehicle only or untreated) was not specified. Based on the data (for lung tumors) provided, it appears that the untreated controls we used, which is the least appropriate for statistical analysis.

HERO ID: 94473 Table: 2 of 2

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Study Citation: Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic

and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

**Health** Cancer/Carcinogenesis

**Outcome(s):** 

Reported Health

Tumor initiation assay: Skin, lung, stomach tumors

**Effect(s):** 

**Duration:** Chronic (>91 days) Chronic; 3x weekly Dermal Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94473

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	High	Although there were deficiencies in test methods, and details provided, data reporting
				was adequate for the outcome of interest.

# Overall Quality Determination

# Uninformative

HERO ID: 1937626 Table: 1 of 6

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Study Citation:	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic;				
Health Outcome(s):	Nutritional/I	Metabolic; Nutritional/Metabolic; Nutrition	al/Metabolic;		
Reported Health	Nutritional/	Metabolic: Body weights; Nutritional/Metal	holic: Rody weig	hts: Nutritional/Metabolic: Rody weights:	
Effect(s):	1 vati ti onal/1	victabolic. Body weights, ivatilional/wictal	bolic. Body weig	ins, Nutritional/Metabolic. Body weights,	
Duration:	Chronic (>9	01 days) 17 weeks - rats			
Chemical:		pethane- Isomer: 1,2-Dichloroethane			
HERO ID:	1937626	,			
Domain		Metric	Rating	Comments	
Domain 1: Test Substan	ce				
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-dichloroethane.	
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.	
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,2-dichloroethane was > 99%.	
Domain 2: Test Design					
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.	
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.	
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.	
Domain 2: Evnogura Ch	orostorization				
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.	
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided.	
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 100 ppm exposure was reported (99.7 ppm); the reported analytical concentration was within 10% of the target concentration.	
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 17 weeks).	
		Conti	inued on next pa	age	

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**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

**Health** Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic;

**Outcome(s):** 

**Reported Health** Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;

Effect(s):

**Duration:** Chronic (>91 days) 17 weeks - rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Nutritional/Metabolic: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to affect any of the outcomes examined.; Nutritional/Metabolic: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality.; Nutritional/Metabolic: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to elicit effects on any of the outcomes evaluated.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.
Domain 4: Test Animals	<b>.</b>			
	Metric 13:	Test Animal Characteristics	Medium	Nutritional/Metabolic: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 8.; Nutritional/Metabolic: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 9.; Nutritional/Metabolic: The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and of the animals were not reported. Starting body weights were presented graphically in Figure 10.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	Nutritional/Metabolic: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Nutritional/Metabolic: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group are typically recommended for subchronic studies).; Nutritional/Metabolic: The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.

### Domain 5: Outcome Assessment

<b>Study Citation:</b>	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.
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Health

Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic;

Outcome(s): Reported Health

Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;

Effect(s):

**Duration:** Chronic (>91 days) 17 weeks - rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	High	Nutritional/Metabolic: The study indicated that body weights were repeated monitored during the study period. Based on the body weight data presented graphically (Figure 8), body weights were recorded weekly.; Nutritional/Metabolic: The study indicated that body weights were repeated monitored during the study period. Based on the body weight data presented graphically (Figure 9), body weights were recorded weekly.; Nutritional/Metabolic: The study indicated that body weights were repeated monitored during the study period. Based on the body weight data presented graphically (Figure 10), body weights were recorded weekly.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Based on data presented graphically, it appeared that body weights were measured at the same time points in treated rats and controls.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Body weights were monitored in all animals.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Medium	All Outcomes: Body weight data for controls were shown graphically.
Domain 6: Confound	ding / Variable Co	ntrol		
Bonian o. Comoun	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not performed / not necessary (negative findings across groups; a 10% benchmark could be used to identify a biologically significant effect).
	Metric 24:	Reporting of Data	Medium	Nutritional/Metabolic: Body weight data were not explicitly reported in the text (other than a statement that there were no clinical signs or pathological changes) and quantitatively in Figure 8. It would be difficult to determine if there was a biologically significant change (>10%) in body weights based on the graph; however, negative results were reported. Data for males and females were not provided separately.; Nutritional/Metabolic: Body weight data were not explicitly reported in the text (other than a statement that there were no clinical signs or pathological changes) and quantitatively in Figure 9. It would be difficult to determine if there was a biologically significant change (>10%) in body weights based on the graph; however, negative results were reported. Data for males and females were not provided separately.; Nutritional/Metabolic: Body weight data were not explicitly reported in the text (other than a statement that there were no clinical signs or pathological changes) and quantitatively in Figure 10. It would be difficult to determine if there was a biologically significant change (>10%) in body weights based on the graph; however, negative results were reported. Data for males and females were not provided separately.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 1937626 Table: 1 of 6

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Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** 

Health Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic;

**Outcome(s):** 

Reported Health Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;

Effect(s):

**Duration:** Chronic (>91 days) 17 weeks - rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain Metric Rating Comments

**Overall Quality Determination** Medium

Study Citation:	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.
Health	Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Hepatic/Liver; Renal/Kidney;
Outcome(s):	
Reported Health	Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver:
Effect(s):	Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;
<b>Duration:</b>	Chronic (>91 days) 17 weeks - rabbits
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1937626

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,2-dichloroethane was > 99%.
Domain 2: Test Design				
S	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 100 ppm exposure was reported (99.7 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 17 weeks).
		Cont	inued on next pa	ge

Study Citation: Health Outcome(s): Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Hepatic/Liver; Renal/Kidney;

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;

**Duration:** Chronic (>91 days) 17 weeks - rabbits

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Metric Rating Comments Domain Number of Exposure Groups Hepatic/Liver: The study evaluated exposure to 1,2-DCA at one concentration (i.e., Metric 11: Medium one exposure group plus the control group). This concentration was chosen based on Dose/Concentration Spacing a previous study at a higher concentration that induced mortality.; Hepatic/Liver: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to affect any of the outcomes examined.; Renal/Kidney: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to affect any of the outcomes examined.; Renal/Kidney: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality.; Hepatic/Liver: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to elicit effects on any of the outcomes evaluated.; Renal/Kidney: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to affect any of the outcomes examined. Metric 12: Exposure Route and Method Medium All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

Study Citation: Health Outcome(s): Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Hepatic/Liver; Renal/Kidney;

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;

**Duration:** Chronic (>91 days) 17 weeks - rabbits

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

190,020			
	Metric	Rating	Comments
Metric 13:	Adequacy and Consistency of Animal	Medium	Hepatic/Liver: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 9.; Hepatic/Liver: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 8.; Renal/Kidney: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 8.; Renal/Kidney: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 9.; Hepatic/Liver: The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and of the animals were not reported. Starting body weights were presented graphically in Figure 10.; Renal/Kidney: The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and of the animals were not reported. Starting body weights were presented graphically in Figure 10.  All Outcomes: Husbandry conditions
	Husbandry Conditions		some information about the diet and water availability (ad libitum).
	Metric 13:  Metric 14:	Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal	Metric 13: Test Animal Characteristics Medium  Metric 14: Adequacy and Consistency of Animal Low

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Health Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Hepatic/Liver; Renal/Kidney; Outcome(s): Reported Health Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Effect(s): Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; **Duration:** Chronic (>91 days) 17 weeks - rabbits Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane **HERO ID:** 1937626 Metric Rating Comments Domain Metric 15: Number of Animals per Group Low Hepatic/Liver: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group would typically be recommended).; Hepatic/Liver: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group would typically be recommended for rodent studies).; Renal/Kidney: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group would typically be recommended for rodent studies).; Renal/Kidney: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group would typically be recommended).; Hepatic/Liver: The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.; Renal/Kidney: The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects. Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology High Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: serum ALT and AST, bromsulphthalein test, liver weight, and liver histology.; Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: serum ALT and AST, liver weight, and liver histology.; Renal/Kidney: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: BUN and serum creatinine, urinary status (parameters not specified, kidney weights, and kidney histology.; Renal/Kidney: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: BUN and serum creatinine, urinary status (parameters not specified, kidney weights, and kidney histology.; Hepatic/Liver: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: serum ALT and AST, bromsulphthalein test, liver weight, and liver histology.; Renal/Kidney: The outcome assessment addressed the outcome of interest. The following assessments of liver toxicity were performed: BUN and serum creatinine, urinary status (parameters not specified, kidney weights, and kidney histology.

Study Citation: Health Outcome(s): Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Hepatic/Liver; Renal/Kidney; Renal/Kidney; Hepatic/Liver; Renal/Kidney;

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;

**Duration:** Chronic (>91 days) 17 weeks - rabbits

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Medium	Hepatic/Liver: The results (Figure 9) show that the activities of liver enzymes were measured for both the group exposed to 1,2-DCA and the controls at the same time points throughout the experiment. The text indicates that bromsulphthalein retention, liver weight, and liver histology were assessed in all animals after 17 weeks exposure.; Hepatic/Liver: The results (Figure 8) show that the activities of liver enzymes were measured for both the group exposed to 1,2-DCA and the controls at the same time points throughout the experiment. The text indicates that liver weight and liver histology were assessed in all animals after 17 weeks exposure.; Renal/Kidney: The results (Figure 8) show that BUN and serum creatinine were measured for both the group exposed to 1,2-DCA and the controls at the same time points throughout the experiment. The text indicates that kidney weight and kidney histology were assessed in all animals after 17 weeks exposure.; Renal/Kidney: The results (Figure 9) show that BUN and serum creatinine were measured for both the group exposed to 1,2-DCA and the controls at the same time points throughout the experiment. The text indicates that kidney weight and kidney histology were assessed in all animals after 17 weeks exposure.; Hepatic/Liver: The results (Figure 10) show that the activities of liver enzymes were measured for both the group exposed to 1,2-DCA and the controls at the same time points throughout the experiment. The text indicates that bromsulphthalein retention, liver weight, and liver histology were assessed in all animals after 17 weeks exposure.; Renal/Kidney: The results (Figure 10) show that BUN and serum creatinine were measured for both the group exposed to 1,2-DCA and the controls at the same time points throughout the experiment. The text indicates that kidney weight and kidney histology were assessed in all animals after 17 weeks exposure.; Renal/Kidney: The results (Figure 10) show that BUN and serum creatinine were measured for both the group exposed to 1,2-DCA and the
	Metric 18:	Sampling Adequacy	High	Hepatic/Liver: Liver endpoints were presumably monitored in all animals.; Hepatic/Liver: Liver endpoints were presumably monitored in all animals.; Renal/Kidney: Renal endpoints were presumably monitored in all animals.; Renal/Kidney: Renal endpoints were presumably monitored in all animals.; Hepatic/Liver: Liver endpoints were presumably monitored in all animals.; Renal/Kidney: Renal endpoints were presumably monitored in all animals.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for these outcomes.

**Study Citation:** Health

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Hepatic/Liver; Renal/Kidney;

Outcome(s):

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were

HERO ID: 1937626 Table: 2 of 6

"always normal").;

**Duration:** Chronic (>91 days) 17 weeks - rabbits

Chemical: 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane

**HERO ID:** 1937626

Domain	Metric	Rating	Comments
Metric 20:	Negative Control Response	Low	Hepatic/Liver: The activities of liver enzymes in controls were shown graphically. The incidence of histopathological lesions in controls was not reported (but presumed to be low). The value for bromsulphthalein retention in controls was reported in the legend of Figure 9.; Hepatic/Liver: The activities of liver enzymes in controls were shown graphically. The incidence of histopathological lesions in controls was not reported (but presumed to be low).; Renal/Kidney: Levels of BUN and serum creatinine in controls were shown graphically. The incidence of histopathological lesions in controls was not reported (but presumed to be low).; Renal/Kidney: Levels of BUN and serum creatinine in controls were shown graphically. The incidence of histopathological lesions in controls was not reported (but presumed to be low).; Hepatic/Liver: The activities of liver enzymes in controls were shown graphically. The incidence of histopathological lesions in controls was not reported (but presumed to be low). The value for bromsulphthalein retention in controls was reported in the legend of Figure 10.; Renal/Kidney: Levels of BUN and serum creatinine in controls were shown graphically. The incidence of histopathological lesions in controls was not reported (but presumed to be low).
Domain 6: Confounding / Variable Con Metric 21:		Medium	All Outcomes: Penerted information did not identify differences among study groups
WEITIC 21:	Confounding Variables in Test Design and Procedures	Mediuiii	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.

Study Citation: Health Outcome(s): Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Hepatic/Liver; Renal/Kidney;

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;

HERO ID: 1937626 Table: 2 of 6

**Duration:** Chronic (>91 days) 17 weeks - rabbits

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Metric Rating Comments Domain N/A Hepatic/Liver: Statistical analysis was not performed/not necessary. Based on the infor-Metric 23: Data Presentation and Analysis mation reported, there were no clinical signs and pathological changes from exposure to 1,2-DCA, including no effects on liver enzymes, bromsulphthalein test, liver weights, or liver histology (clearly negative findings across groups).; Hepatic/Liver: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical signs and pathological changes from exposure to 1,2-DCA, including no effects on liver enzymes, liver weights, or liver histology (clearly negative findings across groups).; Renal/Kidney: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical signs, pathological changes from exposure to 1,2-DCA, including no effects on BUN or serum creatinine, urinary status, kidney weights, or kidney histology (clearly negative findings across groups).; Renal/Kidney: Statistical analysis was not performed/not necessary for most endpoints, based on negative findings for serum creatinine, urinary status, and kidney weights. The study noted that increased BUN and kidney histology were observed in one exposed rabbit (presumably compared to 0/4 controls; ns).; Hepatic/Liver: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical signs and pathological changes from exposure to 1,2-DCA, including no effects on liver enzymes, bromsulphthalein test, liver weights, or liver histology (clearly negative findings across groups).; Renal/Kidney: Statistical analysis was not performed/not necessary. Based on the information reported, there were no clinical signs, pathological changes from exposure to 1,2-DCA, including no effects on BUN or serum creatinine, urinary status, kidney weights, or kidney histology (clearly negative findings across

#### Continued on next page ...

groups).

Study Citation: Health Outcome(s): Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Hepatic/Liver; Renal/Kidney;

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").;

**Duration:** Chronic (>91 days) 17 weeks - rabbits

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain Metric Rating Comments

Metric 24: Reporting of Data Medium

Hepatic/Liver: Data for liver enzymes were reported qualitatively in the text (i.e., there were no pathological changes) and quantitatively in Figure 9. The line graphs for AST and ALT (Figure 9) include one line for controls and one line for 1,2-DCA exposed animals. It would be difficult to determine if there was a biologically significant change based on the graphs; however, negative results were reported. The study indicated that examinations at the end of the study showed no pathological findings. Data for males and females were not provided separately.; Hepatic/Liver: Data for liver enzymes were reported qualitatively in the text (i.e., there were no pathological changes) and quantitatively in Figure 8. The line graphs for AST and ALT (Figure 8) include one line for controls and one line for 1,2-DCA exposed animals. It would be difficult to determine if there was a biologically significant change based on the graphs; however, negative results were reported. The study indicated that examinations at the end of the study showed no pathological findings. Data for males and females were not provided separately.; Renal/Kidney: Data for BUN and serum creatinine were reported qualitatively in the text (i.e., there were no pathological changes) and quantitatively in Figure 8. The line graphs for BUN and serum creatinine (Figure 8) include one line for controls and one line for 1,2-DCA exposed animals. It would be difficult to determine if there was a biologically significant change based on the graphs; however, negative results were reported. The study indicated that examinations at the end of the study showed no pathological findings. Data for males and females were not provided separately.; Renal/Kidney: Data for BUN and serum creatinine were reported qualitatively in the text and quantitatively in Figure 9. The text indicated that there was no "significant" deviations from controls (unclear what significant means in this context since it does not appear that statistics were performed) and that one rabbit showed increased BUN and kidney histology (presumably 1/4 exposed rabbits vs. 0/4 controls; ns). Data for males and females were not provided separately.; Hepatic/Liver: Data for liver enzymes were reported qualitatively in the text (i.e., there were no pathological changes) and quantitatively in Figure 10. The line graphs for AST and ALT (Figure 9) include one line for controls and one line for 1,2-DCA exposed animals. It would be difficult to determine if there was a biologically significant change based on the graphs; however, negative results were reported. The study indicated that examinations at the end of the study showed no pathological findings. Data for males and females were not provided separately.; Renal/Kidney: Data for BUN and serum creatinine were reported qualitatively in the text (i.e., there were no pathological changes) and quantitatively in Figure 8. The line graphs for BUN and serum creatinine (Figure 10). The graphs include one line for controls and one line for 1,2-DCA exposed animals. It would be difficult to determine if there was a biologically significant change based on the graphs; however, negative results were reported. The study indicated that examinations at the end of the study showed no pathological findings. Data for males and females were not provided

Human Health Hazard Animal Toxicology Evaluation HERO ID: 1937626 Table: 2 of 6

### ... continued from previous page

Study Citation: Health Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Hepatic/Liver; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Hepatic/Liver; Renal/Kidney;

Outcome(s):

**Reported Health** Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and

serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were "always normal").; Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a statement indicating that results were

"always normal").;

**Duration:** Chronic (>91 days) 17 weeks - rabbits

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain Metric Rating Comments

## Overall Quality Determination Medium

G. I G. I	H.f., and H.T. Dinnaid, H. Liba, D. (1971). On inhabitant miles of 1.1 and 1.2 dishbarraham. Analysis: Traditable in 27/2 (A):240-245
Study Citation	Hofmann H. T. Birnstiel H. Jobst P (1971). On inhalation foxicity of 1.1- and 1.2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265

Health

Hepatic/Liver; Renal/Kidney;

**Outcome(s):** 

**Reported Health** Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a

statement indicating that results were "always normal").;

Duration: Chemical: Chronic (>91 days) 17 weeks - guinea pigs 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ince			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,2-dichloroethane was $>$ 99%.
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.
D : 2 E (	31			
Domain 3: Exposure C	Metric 7:	D	M - J:	
	Metric /:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 100 ppm exposure was reported (99.7 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 17 weeks).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to affect any of the outcomes examined.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

		continu	ied from previ	ous page			
Study Citation: Health Outcome(s):		Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Hepatic/Liver; Renal/Kidney;					
Reported Health Effect(s):	BUN and se			ulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney d kidney histology. Urine findings evaluated; results not reported (other than			
Duration: Chemical: HERO ID:	Chronic (>9	ordaning that results were always normal )., 01 days) 17 weeks - guinea pigs bethane- Isomer: 1,2-Dichloroethane					
Domain		Metric	Rating	Comments			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF" medical-biological research laboratories;" it is unclear that this is a commercial source The age and starting body weights of the animals were not reported.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).			
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The study used fewer animals per group than would be recommended f studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group woul typically be recommended for rodent studies).			
Domain 5: Outcome A	ssessment						
	Metric 16:	Outcome Assessment Methodology	Medium	Hepatic/Liver: The outcome assessment partially addressed the outcome of interest. T following assessments of liver toxicity were performed based on information presented in the methods: liver weight, and liver histology. No clinical pathology examinations were performed.; Renal/Kidney: The outcome assessment partially addressed the outcome of interest. The following assessments of renal toxicity were performed based or information presented in the methods: kidney weight, and kidney histology. No clinical pathology examinations were performed.			
	Metric 17:	Consistency of Outcome Assessment	High	Hepatic/Liver: Liver weight and histology were assessed at the end of the 17-week stuperiod.; Renal/Kidney: Kidney weight and histology were assessed at the end of the 17-week study period.			
	Metric 18:	Sampling Adequacy	High	Hepatic/Liver: Liver endpoints were presumably monitored in all animals.; Renal/Kidney: Renal endpoints were presumably monitored in all animals.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for these outcomes.			
	Metric 20:	Negative Control Response	Low	Hepatic/Liver: Data for liver endpoints in control animals were not provided.; Renal/Kidney: Data for renal endpoints in control animals were not provided.			
Domain 6: Confoundir	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., information on respiration rates).			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences amon groups with respect to outcomes unrelated to exposure.			
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analyses were not performed/ not necessary (clearly negative findings across groups).			

Hepatic/Liver; Renal/Kidney;

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 1937626 Table: 3 of 6

### ... continued from previous page

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. **Study Citation:** 

Health

Outcome(s):

Reported Health Effect(s):

Hepatic/Liver: Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology; Renal/Kidney: BUN and serum creatinine (rats, rabbits, and cats); kidney weights, and kidney histology. Urine findings evaluated; results not reported (other than a

statement indicating that results were "always normal").;

**Duration:** Chronic (>91 days) 17 weeks - guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Medium	Hepatic/Liver: The text indicated that there were no "significant" deviations from controls in liver weights and no pathological changes based on evaluation of animals killed after 17 weeks exposure. Data for males and females were not discussed separately.; Renal/Kidney: The text indicated that there were no "significant" deviations from controls in kidney weights and no pathological changes based on evaluation of animals killed after 17 weeks exposure. Data for males and females were not discussed separately.

Medium **Overall Quality Determination** 

HERO ID: 1937626 Table: 4 of 6

**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Health Mortality; Mortality; Mortality;

**Outcome(s):** 

**Reported Health** Mortality: Mortality: Mortality: Mortality: Mortality: Mortality; Mortality;

Effect(s):

**Duration:** Chronic (>91 days) 17 weeks - rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,2-dichloroethane was > 99%.
Domain 2: Test Desig	rn			
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; how ever, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 100 ppm exposure was reported (99.7 ppm); the reported analytical concentration was within 10% of the target concentration.

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Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

**Health** Mortality; Mortality; Mortality; Mortality;

Outcome(s):

**Reported Health** Mortality: Mortality: Mortality: Mortality: Mortality: Mortality: Mortality: Mortality; Mortality; Mortality: Mort

**Effect(s):** 

**Duration:** Chronic (>91 days) 17 weeks - rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	1,1-Dicilion 1937626	gemane- Isomer. 1,2-Diemoroemane		
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Mortality: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to affect any of the outcomes examined.; Mortality: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality.; Mortality: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration used was not high enough to elicit effects on any of the outcomes evaluated.; Mortality: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to elicit a response on any of the outcomes evaluated.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Mortality: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 8.; Mortality: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 9.; Mortality: The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.; Mortality: The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and of the animals were not reported. Starting body weights were presented graphically in Figure 10.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
		Continu	ued on next pa	ge

		continu	ied from previ	ous page			
Study Citation: Health Outcome(s):	Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Mortality; Mortality; Mortality; Mortality;						
Reported Health Effect(s):	Mortality: M	Iortality; Mortality: Mortality; Mortality: Mo	ortality; Mortali	ty: Mortality;			
Duration: Chemical: HERO ID:	Chronic (>91 days) 17 weeks - rats 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 1937626						
Domain		Metric	Rating	Comments			
	Metric 15:	Number of Animals per Group	Low	Mortality: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Mortality: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group are typically recommended for subchronic studies).; Mortality: The study used fewer animals per group than would be recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group would typically be recommended for rodent studies).; Mortality: The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.			
Domain 5: Outcome A	Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Mortality was presumably measured appropriately (i.e., via active monitoring of the animals' condition).			
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: The time points at which mortality was assessed were not reported.			
	Metric 18:	Sampling Adequacy	High	All Outcomes: Mortality was monitored in all animals.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this outcome.			
	Metric 20:	Negative Control Response	Medium	All Outcomes: Mortality data for control animals was not reported.			
Domain 6: Confoundi	ng / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.			
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not performed / not necessary (negative findings across groups).			
	Metric 24:	Reporting of Data	Medium	All Outcomes: The study indicated that exposed rats tolerated 1,2-DCA exposure without clinical signs (presumably there was no mortality). It was not explicitly stated (but assumed) that there was no mortality in controls.			

# Overall Quality Determination

# Medium

Study Citation: Health Outcome(s):		I. T., Birnstiel, H., Jobst, P. (1971). On inhal matological; Immune/Hematological; Immu		1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.					
Reported Health	Immuna/Ha	Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific							
Effect(s):				plogical: Blood counts - specific parameters not specified (rats, rabbits, and cats					
Effect(s).	only);	not specified (rats, rabbits, and cats only),	minune/Hematt	biogreai. Blood counts - specific parameters not specified (rais, rabbits, and cats					
Duration:	Chronic (>91 days) 17 weeks - rats								
Chemical:		bethane- Isomer: 1,2-Dichloroethane							
HERO ID:	1937626	settlane Isomer. 1,2 Bremoreculaire							
Domain		Metric	Rating	Comments					
Domain 1: Test Substance	ce								
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-dichloroethane.					
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.					
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of 1,2-dichloroethane was > 99%.					
Domain 2: Test Design									
20114111 21 1434 2 433g.1	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.					
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls were not required by study type.					
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.					
Domain 3: Exposure Ch	aracterization								
Domain 3. Exposure Cir	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.					
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: It appeared that exposures were applied consistently across groups; how- ever, limited details were provided.					
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 100 ppm exposure was reported (99.7 ppm); the reported analytical concentration was within 10% of the target concentration.					
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 17 weeks).					

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Study Citation: Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Health Immune/Hematological; Immune/Hematological; Immune/Hematological;

**Outcome(s):** 

Reported Health Effect(s):

Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats

only);

**Duration:** Chronic (>91 days) 17 weeks - rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

HERO ID:	193/626				
Domain		Metric	Rating	Comments	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing		Medium	Immune/Hematological: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to affect any of the outcomes examined.; Immune/Hematological: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality.; Immune/Hematological: The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to elicit effects on any of the outcomes evaluated.	
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The study stated that dynamic air chambers were used without indicating the number of air changes.	
Domain 4: Test Animals					
	Metric 13:	Test Animal Characteristics	Medium	Immune/Hematological: The species, strain, and sex of the test animals were reported (male and female Sprague-Dawley rats). The source was indicated as "breeding of Gassner;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 8.; Immune/Hematological: The species, strain, and sex of the test animals were reported (male and female Bunte rabbits). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age of the animals was not reported. Starting body weights were presented graphically in Figure 9.; Immune/Hematological: The species and sex of the test animals were reported (male and female cats). The source was indicated as "breeding of BASF's medical-biological laboratories;" it is unclear that this is a commercial source. The age and of the animals were not reported. Starting body weights were presented graphically in Figure 10.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).	
	Metric 15:	Number of Animals per Group	Low	Immune/Hematological: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 rats/sex, when at least 10/sex/group are typically recommended for subchronic studies).; Immune/Hematological: The study used fewer animals per group than that recommended for studies of this type (i.e., there were 2 rabbits/sex, when at least 5/sex/group are typically recommended for subchronic studies).; Immune/Hematological: The study used 2 cats/sex/group. Although this number of animals may be considered sufficient based on the species, the few numbers of animals per group makes it more difficult to characterize toxicological effects.	

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**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

Health

Effect(s):

Outcome(s):

**Reported Health** 

Immune/Hematological; Immune/Hematological; Immune/Hematological;

Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats only); Immune/Hematological: Blood counts - specific parameters not specified (rats, rabbits, and cats

only);

**Duration:** Chronic (>91 days) 17 weeks - rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain	Metric		Rating	Comments
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The study indicated that blood counts (parameters not specified) were repeatedly monitored during the experimental period.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: The time points in which hematology parameters were evaluated were not reported.
	Metric 18:	Sampling Adequacy	Medium	All Outcomes: Blood counts were presumably measured in all animals.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Medium	All Outcomes: The study authors indicated that results for controls were normal.
Domain 6: Confoundir	~	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not performed/not necessary. The study reported that blood counts were "always normal" (clearly negative findings across groups).
	Metric 24:	Reporting of Data	Medium	All Outcomes: Negative results were reported qualitatively. The study indicated that there were no "clinical signs" or "pathological changes" compared to controls and that blood counts were "always normal."

# **Overall Quality Determination**

# Medium

1,1-Dichloroethane

**Study Citation:** 

Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265.

HERO ID: 1937626 Table: 6 of 6

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights

Effect(s):

**Duration:** Chronic (>91 days) 17 weeks - guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance source was reported as "Dr. Schuchardt GmbH;" it is not clear that the test substance was obtained from a commercial source. The test substance was analytically determined via a colorimetric method.
	Metric 3:	Test Substance Purity	High	The purity of 1,2-dichloroethane was > 99%.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	The study noted that equally large groups of test animals received the same volume of air without dichloroethane; this group served as the control.
	Metric 5:	Positive Controls	N/A	Positive controls were not required by study type.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	The study indicated that the test substance (in liquid form) was fed to a steel evaporator by means of an infusion apparatus; vapors were absorbed by a metered air steam and passed into two parallel chambers (200 L each). The specific equipment and methods (e.g., elevated temperature or bubbler) used to generate vapors were not reported. Given that the test substance was analytically verified in the inhalation chamber, any omissions are not expected to substantially impact the study results.
	Metric 8:	Consistency of Exposure Administration	Medium	It appeared that exposures were applied consistently across groups; however, limited details were provided.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The study indicated that the repeated analytical determination of 1,2-dichloroethane in the inhalation chamber was colorimetric according to the principle of the Fujiwara reaction (GC was not used). The analytical concentration associated with the 100 ppm exposure was reported (99.7 ppm); the reported analytical concentration was within 10% of the target concentration.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency/duration was appropriate (6 hours/day, 5 days/week, for 17 weeks).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Missing Conf	The study evaluated exposure to 1,2-DCA at one concentration (i.e., one exposure group plus the control group). This concentration was chosen based on a previous study at a higher concentration that induced mortality. The concentration tested was not high enough to affect any of the outcomes examined.
	Metric 12:	Exposure Route and Method	Medium	The study stated that dynamic air chambers were used without indicating the number of air changes.

Domain 4: Test Animals

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**Study Citation:** Hofmann, H. T., Birnstiel, H., Jobst, P. (1971). On inhalation toxicity of 1,1- and 1,2-dichloroethane. Archiv für Toxikologie 27(3-4):248-265. Nutritional/Metabolic

Health

**Outcome(s): Reported Health** 

Body weights

Effect(s):

**Duration:** Chronic (>91 days) 17 weeks - guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1937626

Domain		Metric	Rating	Comments
	Metric 13:	Metric 13: Test Animal Characteristics		The species, strain, and sex of the test animals were reported (male and female Pirbright-White guinea pigs). The source was indicated as "breeding of BASF's medical-biological research laboratories;" it is unclear that this is a commercial source. The age and starting body weights of the animals were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were largely not reported. The study provided some information about the diet and water availability (ad libitum).
	Metric 15:	Number of Animals per Group	Low	The study used fewer animals per group than that recommended for studies of this type (i.e., there were 5 guinea pigs/sex, when at least 10/sex/group are typically recommended for subchronic studies).
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	The study indicated that body weights were repeated monitored during the study period.
	Metric 17:	Consistency of Outcome Assessment	Low	The time points at which body weights were evaluated were not specified.
	Metric 18:	Sampling Adequacy	High	Body weights were monitored in all animals.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Low	Body weight data for controls were not reported.
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among study groups with respect to confounding factors; however, limited information was provided (e.g., no information on respiration rates).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to indicate that there were differences among groups with respect to outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not performed / not necessary (negative findings across groups; a 10% benchmark could be used to identify a biologically significant effect).
	Metric 24:	Reporting of Data	Medium	Body weight data were not explicitly reported in the text (other than a statement that there were no clinical signs or pathological changes). Data for males and females were not provided separately.

# **Overall Quality Determination**

# **Medium**

Study Citation:	IRFMN, (1976). Clinical chemistry results after 6 months inhalatory exposure to ethylene dichloride.
Health	Hepatic/Liver; Renal/Kidney; Immune/Hematological;
Outcome(s):	

Reported Health

Hepatic/Liver: Related clinical chemistry (Bilirubin measurements); Renal/Kidney: Related clinical chemistry (BUN, electrolytes); Urinalysis; Im-

**Effect(s):** mune/Hematological: Hematology, and serum immunoglobulins;

**Duration:** Chronic (>91 days) 6 months

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447359

Domain	Metric		Rating	Comments		
Domain 1: Test Substan	ce					
	Metric 1:	Metric 1: Test Substance Identity		All Outcomes: The test substance was identified as ethylene dichloride (EDC); a CASRN was provided on the cover sheet of the OTS report, but did not appear in the main document.		
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test material was reported in a related document (HERO ID 5447356). A lot and/or batch number was not provided.		
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity was clearly reported (99.55% pure), and impurities were listed: Trichloroethylene (0.11%) and benzene (0.34%)		
Domain 2: Test Design						
C	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Negative control animals were exposed to air only under the same experimental conditions.		
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not necessary for this study type.		
_	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.		
Domain 3: Exposure Ch	aracterization					
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: There was no mention of the method and equipment used to generate the test substance.		
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported (see examples in header) and the missing information is likely to have a substantial impact on results.		
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: The exposure doses/concentrations or amounts of test substance were reported but with substantial ambiguity about precision (e.g., only target concentrations instead of analytical measurements). Additionally, the exposure concentration in the high exposure group was lowered from 250 ppm to 150 ppm. Another HERO ID (5447364) mentioned that the change occurred after 12 weeks, however this was not specified in the current report.		
	Metric 10:	Metric 10: Exposure Frequency and Duration		All Outcomes: Typical exposures for a chronic duration study is 6 hrs/day, 5/days per week. This study exposed animals for 7 hrs/day, 5/days per week. This is unlikely to have a substantial impact on the study results.		
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: No justification was provided for the selected exposure concentrations. The highest concentration (250 ppm) resulted in acute toxicity and was reduced to 150 ppm "after a few weeks." The number of groups was adequate.		
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Only very minimal if any details about the methods for inhalation exposure administration (as described above) were reported, resulting in significant uncertainty about the true exposure parameters.		
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		continu	ied from previ	ous page				
Study Citation: Health Outcome(s):	IRFMN, (1976). Clinical chemistry results after 6 months inhalatory exposure to ethylene dichloride. Hepatic/Liver; Renal/Kidney; Immune/Hematological;							
Reported Health Effect(s): Duration: Chemical: HERO ID:	Hepatic/Liver: Related clinical chemistry (Bilirubin measurements); Renal/Kidney: Related clinical chemistry (BUN, electrolytes); Urinalysis; Immune/Hematological: Hematology, and serum immunoglobulins; Chronic (>91 days) 6 months 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 5447359							
Domain		Metric	Rating	Comments				
Domain 4: Test Anima	ale.							
Domain 4. Test Allina	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Animal species, strain, sex, and age (age is reported in HERO 5447364) were reported. Based on the available information, these rats were likely an in-house colony. Starting body weights were not provided.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not sufficiently reported to evaluate if husbandry was adequate and whether differences occurred between control and exposed populations. These deficiencies are likely to have a substantial impact on results.				
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals per group was not explicitly stated. Based on the available data tables, at least 7-8 animals/sex/group were exposed. This is less than the recommended 20/sex/group (OECD 452)				
Domain 5: Outcome A	ssessment							
Bollian 3. Outcome 1	Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: This study only includes a reporting of serum chemistry, hematology, and urinalysis endpoints, most of which fall into the liver, kidney, or immunological/hematological target organs/systems. As stand-alone endpoints these are not considered the most sensitive endpoints for these outcomes and are usually reported in conjunction with organ weight and/or histopathology data. Based on data available from linked/related HERO IDs, organ weights were not measured, and histopathology focused on tumor incidences.				
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were not reported. The dates of the blood draws were not specified, only that the data follows 6 months of exposure.				
	Metric 18:	Sampling Adequacy	High	All Outcomes: The sampling was adequate to allow statistical analysis of the data.				
	Metric 19:	Blinding of Assessors	High	All Outcomes: The study indicated that assessors were blinding, although this is not typically necessary for clinical chemistry, hematology, and urinalysis endpoints.				
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were appropriate for the outcomes of interest.				
Domain 6: Confoundin	ng / Variable Co	ntrol						
Domain o. Comoundin	Metric 21:	Confounding Variables in Test Design	Low	All Outcomes: body weight changes, food/water intake, and respiratory rates were not				
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	reported. The test substance is considered to be a respiratory irritant.  All Outcomes: Available information (hematological and serum chemistry analysis that would detect the presence of infection), did not indicate that there were any health outcomes (e.g., infection) unrelated to exposure in any group. No other possible health outcomes were reported.				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were described and were appropriate for the outcomes of interest.				
		Continu	ued on next pa	nge				

HERO ID: 5447359 Table: 1 of 1

1,1-Dichloroethane

### ... continued from previous page

IRFMN, (1976). Clinical chemistry results after 6 months inhalatory exposure to ethylene dichloride. **Study Citation:** 

Health

Hepatic/Liver; Renal/Kidney; Immune/Hematological;

**Outcome(s):** 

Reported Health Hepatic/Liver: Related clinical chemistry (Bilirubin measurements); Renal/Kidney: Related clinical chemistry (BUN, electrolytes); Urinalysis; Im-

Effect(s): mune/Hematological: Hematology, and serum immunoglobulins;

**Duration:** Chronic (>91 days) 6 months

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5447359

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	High	All Outcomes: The data were adequately reported. Individual animal data were provided
				along with means and a measure of variance.

# **Overall Quality Determination**

# Medium

**Study Citation:** 

IRFMN, (1978). Clinical chemistry results in adult rats exposed to ethylene dichloride by inhalation for 12 months.

Health

Immune/Hematological; Hepatic/Liver; Renal/Kidney;

**Outcome(s):** 

**Reported Health Effect(s):** 

Immune/Hematological: Hematology, serum alpha 2, alpha 2, and beta globulins, urinary mucus, epithelial cells and microorganisms, urinary leukocytes, erythrocytes.; Hepatic/Liver: Serum glucose, bilirubin, total protein, GOT, LDH, GPT, ALP, albumin, gamma GT; Renal/Kidney: BUN, CPK, Na, K, Ca,

HERO ID: 5447364 Table: 1 of 1

IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.;

**Duration: Chemical:**  Chronic (>91 days) 12-Months

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 

5447364

Domain	Domain Metric		Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test material was identified as ethylene dichloride (EDC); CASRN 107-06-2
	Metric 2:	Test Substance Source	Low	All Outcomes: The source was provided; a batch and/or lot number was not specified.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity was reported (99.82%) and impurities were listed. These included 1,1-ethylene dichloride (0.02%), CCL4 (0.02%), benzene (0.09%), trichloroethylene (0.02%), and perchloroethylene (0.03%)
Domain 2: Test Design				
J	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Negative controls were exposed to air only under the same experimental conditions.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly assigned to study groups, the method of randomization was not specified.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: There was no mention of the method and equipment used to generate the test substance.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported (see examples in header) and the missing information is likely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The exposure doses/concentrations or amounts of test substance were reported but with substantial ambiguity about precision (e.g., only an estimated range AND only nominal instead of analytical measurements).
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Animals were exposed 7 hrs/day, 5 days/week; 6 hrs/day is typical, but this is unlikely to have a substantial impact on results.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The number of exposure groups was adequate. The highest exposure concentration had to be decreased a few weeks after the start of exposure due to acute toxicity.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Some details of the exposure methods were provided in HERO ID 094773. Animals were exposed whole-body in stainless steel/glass chambers with no more than 270 animals per chamber. No details on whether the chambers were static or dynamic were provided.

Domain 4: Test Animals

### ... continued from previous page

**Study Citation:** IRFMN, (1978). Clinical chemistry results in adult rats exposed to ethylene dichloride by inhalation for 12 months. Health Immune/Hematological; Hepatic/Liver; Renal/Kidney; **Outcome(s):** Immune/Hematological: Hematology, serum alpha 2, alpha 2, and beta globulins, urinary mucus, epithelial cells and microorganisms, urinary leukocytes, Reported Health Effect(s): erythrocytes.; Hepatic/Liver: Serum glucose, bilirubin, total protein, GOT, LDH, GPT, ALP, albumin, gamma GT; Renal/Kidney: BUN, CPK, Na, K, Ca, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.; **Duration:** Chronic (>91 days) 12-Months 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical: HERO ID:** 5447364

Domain	Metric	Rating	Comments
Metric 13:	Test Animal Characteristics	Low	All Outcomes: Animal species, strain, age, and sex were reported. Starting body weights were not provided. Based on the information provided animals may have been from an in-house colony. Animals were 14 months at the start of the study, this age may not be appropriate for a 12-month study duration unless the focus of the study was to look at exposure effects in older animals.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Immune/Hematological: Some animal husbandry conditions were provided in HERO ID 094773 including food and water availability, cage details, and room temperature. Animals were housed ten per cage. Humidity and light cycle were not specified. No differences were noted across groups.; Hepatic/Liver: Some animal husbandry conditions were provided in HERO ID 094773 including food and water availability, cage details, and room temperature. Animals were housed ten per cage. Humidity and light cycle were not specified. No differences were noted across groups.; Renal/Kidney: The number of animals per group was not explicitly reported. 8-10 animals/sex/group were sacrificed at 12 months. It is unclear if this was the number of animals exposed or just the number of animals sampled. If this was the number of animals treated per group, it is less than recommended for a chronic study.
Metric 15:	Number of Animals per Group	Low	Immune/Hematological: The number of animals per group was not explicitly reported. 8-10 animals/sex/group were sacrificed at 12 months. It is unclear if this was the number of animals exposed or just the number of animals sampled. If this was the number of animals treated per group, it is less than recommended for a chronic study.; Hepatic/Liver: The number of animals per group was not explicitly reported. 8-10 animals/sex/group were sacrificed at 12 months. It is unclear if this was the number of animals exposed or just the number of animals sampled. If this was the number of animals treated per group, it is less than recommended for a chronic study.; Renal/Kidney: The number of animals per group was not explicitly reported. It appears there is data for 7-8 animals/sex/group. It is unclear if this was the number of animals exposed, or just the number of animals sampled. If this was the number of animals treated per group, it is less than recommended for a chronic study.
Domain 5: Outcome Assessment Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: The outcome assessment methodology was clearly reported. This reference only reports interim clinical chemistry, hematology, and urinalysis results. These endpoints are not sensitive for determining organ-specific toxicity and typically would be grouped with organ weight data and histopathology.
Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details regarding the execution of the study protocol for outcome assessment were provided. Blood was collected at the 12-month terminal sacrifice.
Metric 18:	Sampling Adequacy	High	All Outcomes: The number of animals sampled (7 or 8) was adequate for statistical analysis of the dataset.

		continu	ied from previ	ous page				
Study Citation: Health Outcome(s):	Immune/Her	IRFMN, (1978). Clinical chemistry results in adult rats exposed to ethylene dichloride by inhalation for 12 months. Immune/Hematological; Hepatic/Liver; Renal/Kidney;						
Reported Health Effect(s):	erythrocytes	Immune/Hematological: Hematology, serum alpha 2, alpha 2, and beta globulins, urinary mucus, epithelial cells and microorganisms, urinary leukocytes, erythrocytes.; Hepatic/Liver: Serum glucose, bilirubin, total protein, GOT, LDH, GPT, ALP, albumin, gamma GT; Renal/Kidney: BUN, CPK, Na, K, Ca, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.;						
<b>Duration:</b>		1 days) 12-Months	ŕ					
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	5447364							
Domain		Metric	Rating	Comments				
	Metric 19: Blinding of Assessors		N/A	All Outcomes: Assessors were blinded to the treatment groups during analysis., although this is not typically necessary for the endpoints measured (e.g., clinical chemistry and hematology).				
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate				
Domain 6: Confoundi	ing / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: The study did not report information to determine confounding (i.e, not body weights or food or water intake. Respiratory rates were not reported, and the test material is expected to be a respiratory irritant.				
	Metric 22: Health Outcomes Unrelated to Exposure		Medium	All Outcomes: Details regarding animal attrition and health outcomes unrelated to exposure (e.g., infection) were reported for each study group and there were no differences among groups that could influence the outcome assessment. Blood work was not suggestive of the presence of infection.				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed, with some methods described. Sufficient data were provided to conduct an independent statistical analysis.				
	Metric 24:	Reporting of Data	High	All Outcomes: The data were adequately reported, including individual animal data and means with a measure of variance.				

# **Overall Quality Determination**

# Medium

HERO ID: 200427 Table: 1 of 5

Human Health Hazard Animal Toxicology Evaluation 1,1-Dichloroethane

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** Tumor incidence

Effect(s):

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ance			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Desig	n			
	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only
	Metric 5:	Positive Controls	Low	A positive control is generally not required for a cancer bioassay, but a PB control for liver tumor formation was included. The text indicates PB produced significant responses at both collection points, however, independent analysis did not find either the incidence at 24 weeks (2/10 vs. 0/10 in controls), or at 52 weeks (9/25 vs. 5/25) to reach statistical significance (Fisher's exact). The only significant positive response appears to be an increase in the number of tumrps/mouse at 52 weeks. Overall, the positive control (in combination with a poor study design) did not appear to adequately show the study was sensitive to detect tumor promotion ability.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure (	Tharacterization			
Domain 3. Exposure C	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflon stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
	Metric 9:	Administration Reporting of Doses/Concentrations	High	The doses were reported in mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group, the study Authors did report an Approximate weekly dose mg/kg body weight, however, the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.

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**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Cancer/Carcinogenesis Health

**Outcome(s):** 

**Reported Health** Tumor incidence

Effect(s):

**Duration:** 

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	200427			
Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	Uninformative	Animals were exposed continuously via drinking water for up to 52 weeks. This duration is shorter than is acceptable for a standard cancer study in mice (>= 18 months would be considered appropriate for mice) and is inadequate for determining tumorigenicity.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Dose levels were based on preliminary studies and were justified by the study authors. Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three dose levels for a carcinogenicity study
	Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.
Domain 4: Test Anim	ıals			
	Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
	Metric 15:	Number of Animals per Group	Low	The number of animals/group (35 males only/group) was lower than the typical number used in studies of the same or similar type.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Appropriate standard techniques were described for this outcome of interest, although minimal details were provided (e.g., number of samples/tissue, number of slides examined etc.,)
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
	Metric 18:	Sampling Adequacy	Medium	10 animals/sex/group were sampled at 24 weeks, leaving 25 animals/sex/group at the 52-week evaluation. It is unclear if sampling was appropriate since no effects were observed.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
	Metric 20:	Negative Control Response	High	The negative untreated (water only) control group appeared to have an appropriate response.
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Drinking water intake was graphically reported for the experimental, and control groups (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text discusses significant differences in drinking water intake results for other chemicals but does not report results for the COI.

HERO ID: 200427 Table: 1 of 5

### ... continued from previous page

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Cancer/Carcinogenesis

Outcome(s):

Reported Health Tun

Effect(s):

Tumor incidence

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was clearly performed for some endpoints (text reports whether results were significant or not); however, the type of analysis (methods) used are not described.
	Metric 24:	Reporting of Data	High	Tumor incidence data was well documented.

## **Overall Quality Determination**

### Uninformative

HERO ID: 200427 Table: 2 of 5

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice. Environmental Health Perspectives 69:89-95.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** 

Tumor incidence

Effect(s):

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Tumor promotion

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only, and initiator (DENA) only
	Metric 5:	Positive Controls	Medium	PB was included as a positive control for liver tumor formation; the text reports that a significant increase in incidence was observed, it is unclear how this significance was determined as it appears to be incorrect. Incidences at 24 wks were: 7/10 initiated only controls, vs 9/10 those treated with PB, which does not reach significance based on independent review. However, the number of tumors/mouse was significantly increased over controls, and therefore the test was considered valid.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure C	haracterization			
Domain 3. Exposure C	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflon stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
		Administration	S	
	Metric 9:	Reporting of Doses/Concentrations	High	The doses were reported as mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group, the study Authors did report an Approximate weekly dose mg/kg body weight, however, the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were exposed continuously in drinking water for up to 52 weeks. This duration is shorter than is acceptable for a standard cancer study in mice (>= 18 months would be considered appropriate for mice). However, this study also tested the potential for tumor promotion, and the study duration was considered acceptable for this purpose.
		C	ontinued on next page	

Human Health Hazard Animal Toxicology Evaluation HERO ID: 200427 Table: 2 of 5

### ... continued from previous page

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** 

Tumor incidence

Effect(s):

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Tumor promotion **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

200427			
	Metric	Rating	Comments
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Dose levels were based on preliminary studies and were justified by the study authors.  Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three dose levels for a carcinogenicity study
Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.
Ja			
Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
Metric 15:	Number of Animals per Group	Medium	The number of animals/group (35 males only/group) was lower than the typical number used in a standard cancer bioassay, but may be appropriate for a short-duration tumor promotion assay
ssessment			
Metric 16:	Outcome Assessment Methodology	High	Appropriate standard techniques were described for this outcome of interest, although minimal details were provided (e.g., number of samples/tissue, number of slides examined etc.,)
Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
Metric 18:	Sampling Adequacy	Medium	10 animals/sex/group were sampled at 24 weeks, leaving 25 animals/sex/group at the 52 week evaluation. It is unclear if sampling was appropriate since no effects were observed.
Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
Metric 20:	Negative Control Response	Uninformative	The response of the tumor initiator only control group was too strong (72-100% of animals had tumors at 52 weeks), and this precluded the ability to determine whether the test substance could function as a tumor promoter.
ng / Variable Co	ntrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Drinking water intake was graphically reported for the experimental, and control group (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text discusses significant differences in drinking water intake results for other chemicals but does not report results for the COI.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 11:  Metric 12:  Ils  Metric 13:  Metric 14:  Metric 15:  Sssessment  Metric 16:  Metric 17:  Metric 18:  Metric 19:  Metric 20:  Ing / Variable Co  Metric 21:	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group  Sessessment  Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method High  Metric 13: Test Animal Characteristics High  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group Medium  Metric 16: Outcome Assessment Methodology High  Metric 17: Consistency of Outcome Assessment High Metric 18: Sampling Adequacy Medium  Metric 19: Blinding of Assessors N/A Metric 20: Negative Control Response Uninformative  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Medium

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

HERO ID: 200427 Table: 2 of 5

### ... continued from previous page

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Cancer/Carcinogenesis

Outcome(s):

Reported Health

Tumor incidence

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Tumor promotion

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was clearly performed for some endpoints (text reports whether results were significant or not); however, the type of analysis (methods) used are not described.
	Metric 24:	Reporting of Data	High	Tumor incidence data was well documented.

# Overall Quality Determination

### Uninformative

HERO ID: 200427 Table: 3 of 5

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights; water intake

Effect(s):

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay **Duration:** 

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only
	Metric 5:	Positive Controls	N/A	A positive control is generally not required for this endpoint
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure C	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflon stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
		Administration		
	Metric 9:	Reporting of Doses/Concentrations	High	The doses were reported in mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group, the study Authors did report an Approximate weekly dose mg/kg body weight, however, the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously via drinking water for up to 52 weeks. This is acceptable for the endpoint(s) of interest
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Dose levels were based on preliminary studies and were justified by the study authors. Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three-dose levels for a carcinogenicity study, but appropriate for the endpoint of interest.
	Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.

Domain 4: Test Animals

### ... continued from previous page

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice. Environmental Health Perspectives 69:89-95.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Body weights; water intake

Effect(s):

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
	Metric 15:	Number of Animals per Group	Low	The number of animals/group (35 males only/group) was lower than the typical number used in a chronic study, and typically both sexes are preferred.
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Body weights were only recorded monthly and on a per-cage basis. The study does not specify how many mice were per cage. This is not a standard practice for body weight measurements. Drinking water consumption was measured weekly. The mean water intake (in grams) of each mouse per day was calculated by subtracting the weight of water after 1 week from the weight of the water at time of filing and dividing this number by the number of days and the number of mice per cage. This method requires the assumption that each mouse drinks an equivalent amount of water.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
	Metric 18:	Sampling Adequacy	Medium	The study used cage vs. individual for body weight measurements, which is not the preferred experimental unit.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
	Metric 20:	Negative Control Response	High	Untreated mice were reported to show an expected result
Domain 6: Confounding	y / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Drinking water intake was graphically reported for the experimental, and control group (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text reports a statistical significant decrease in drinking water intake from 8 weeks until 48 weeks of treatment compared with the other treatment groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was clearly performed for some endpoints (text reports whether results were significant or not); however, the type of analysis (methods) used are not described, and it appears the comparator group was not always the control groups (e.g statistical comparisons were made between other treatment groups). Data are provided graphically, but not in a manner that easily allows for independent statistical analysis.

HERO ID: 200427 Table: 3 of 5

1,1-Dichloroethane

### ... continued from previous page

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Nutritional/Metabolic

Outcome(s):

**Reported Health** Body weights; water intake

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Low	Data were reported as means without measures of variance; control data were reported
				on separate graphs than the experimental data, making comparisons difficult. The dosing
				(as reported) is not particularly useful, and determining accurate dosing will be difficult
				using the data as presented. Statical analyses were not included in the graphs, although
				the text indicates whether any significant changes were observed.

Overall Quality Determination Medium

HERO ID: 200427 Table: 4 of 5

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only, and DENA (initiator) only
	Metric 5:	Positive Controls	N/A	A positive control is generally not required for this endpoint
_	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure C	haracterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflon stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
		Administration		• •
	Metric 9:	Reporting of Doses/Concentrations	High	The doses were reported in mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group, the study Authors did report an Approximate weekly dose mg/kg body weight, however, the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously via drinking water for up to 52 weeks. This is acceptable for the endpoint(s) of interest
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Dose levels were based on preliminary studies and were justified by the study authors. Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three-dose levels for a carcinogenicity study, but appropriate for the endpoint of interest.
	Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.

#### Domain 4: Test Animals

HERO ID: 200427 Table: 4 of 5

### ... continued from previous page

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

**Effect(s):** 

**Duration:** 

Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

HERO ID:	200427			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
	Metric 15:	Number of Animals per Group	Low	The number of animals/group (35 males only/group) was acceptable for this outcome, however, OECD recommendations for a chronic study indicate both sexes should be evaluated.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Body weights were only recorded monthly and on a per-cage basis. The study does not specify how many mice were per cage. This is not a standard practice for body weight measurements. Drinking water consumption was measured weekly. The mean water intake (in grams) of each mouse per day was calculated by subtracting the weight of water after 1 week from the weight of the water at time of filing and dividing this number by the number of days and the number of mice per cage. This method requires the assumption that each mouse drinks an equivalent amount of water.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
	Metric 18:	Sampling Adequacy	Medium	The study used cage vs. individual for body weight measurements, which is not the preferred experimental unit.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
	Metric 20:	Negative Control Response	High	Untreated mice were reported to show an expected result
Domain 6: Confound	ling / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Drinking water intake was graphically reported for the experimental, and control groups (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text discusses significant differences in drinking water intake results for other chemicals but does not report changes for this COI.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis not described for this outcome, however, incidence data were provided to allow independent analysis.
	Metric 24:	Reporting of Data	Medium	Data were provided in the text. Only results from the high-dose group were clearly reported.

1,1-Dichloroethane HERO ID: 200427 Table: 4 of 5

### ... continued from previous page

**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health Mortality

**Outcome(s):** 

**Reported Health** Survival

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments	
<b>Overall Quality Det</b>	ermination	High		

HERO ID: 200427 Table: 5 of 5

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Hepatic/Liver

**Outcome**(s):

**Reported Health** 

Non-cancer lesions; liver weights

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified by standard nomenclature; CASRNs were not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was provided; the batch and lot number were not reported.
	Metric 3:	Test Substance Purity	Medium	Purity was not explicitly reported, but the test substance was reported to be "glass distilled, with no preservatives"
Domain 2: Test Desi	gn			
	Metric 4:	Negative and Vehicle Controls	High	Negative controls included water only, and DENA (initiator) only
	Metric 5:	Positive Controls	N/A	A positive control is generally not required for this endpoint
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated, but the method of allocation was not reported.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	High	Preparation procedures were reported. The text indicated water bottles contained Teflon stoppers suggesting measures were taken to minimize evaporation. Drinking water was freshly made and changed weekly.
	Metric 8:	Consistency of Exposure	High	Water was available ad libitum across groups
		Administration	_	· ·
	Metric 9:	Reporting of Doses/Concentrations	High	The doses were reported in mg/L (drinking water). Drinking water intake was monitored and reported graphically (data points at 8-week intervals) in g/mouse/day, and mean body weights (g) were also graphically reported in the same intervals. It should be possible to calculate doses in mg/kg/day based on the data provided. For the high dose group, the study Authors did report an Approximate weekly dose mg/kg body weight, however, the footnotes indicate that individual/study-specific water intake and body weights were not used in the determination; instead, the calculation was based on mean daily water uptake for a 30g mouse.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously via drinking water for up to 52 weeks. This is acceptable for the endpoint(s) of interest
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Dose levels were based on preliminary studies and were justified by the study authors. Doses were set to be comparable to those previously used for oral studies. Two experimental groups were tested in addition to the controls. This is lower than the recommended three-dose levels for a carcinogenicity study, but appropriate for the endpoint of interest.
	Metric 12:	Exposure Route and Method	High	Justification for the route of exposure was provided.

Domain 4: Test Animals

HERO ID: 200427 Table: 5 of 5

### ... continued from previous page

Study Citation: Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Health

Hepatic/Liver

**Outcome(s):** 

**Reported Health** 

Non-cancer lesions; liver weights

**Effect(s):** 

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

TIERO ID.	200427			
Domain	3.5 . 1.2	Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	Species, strain, source, age, and sex were reported. Initial body weights at the start of exposure were not explicitly reported, but can be estimated from the provided graphs.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions (cages, bedding, food and water) were reported and were consistent across groups.
	Metric 15:	Number of Animals per Group	Low	The number of animals/group (35 males only/group) was acceptable for this outcome, however, OECD recommendations for a chronic study indicate both sexes should be evaluated.
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Body weights were only recorded monthly and on a per-cage basis. The study does not specify how many mice were per cage. This is not a standard practice for body weight measurements. Drinking water consumption was measured weekly. The mean water intake (in grams) of each mouse per day was calculated by subtracting the weight of water after 1 week from the weight of the water at time of filing and dividing this number by the number of days and the number of mice per cage. This method requires the assumption that each mouse drinks an equivalent amount of water.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent across groups
	Metric 18:	Sampling Adequacy	Medium	The study used cage vs. individual for body weight measurements, which is not the preferred experimental unit.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoints evaluated.
	Metric 20:	Negative Control Response	High	Untreated mice were reported to show an expected result
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Drinking water intake was graphically reported for the experimental, and control groups (although not on the same graph). It is difficult to determine whether there were any palatability issues between treatment groups and controls. The text discusses significant differences in drinking water intake results for other chemicals but does not report changes for this COI.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Uninformative	Statistical analysis was not described for this outcome despite text indicating a positive response. Data were not available for independent analysis
	Metric 24:	Reporting of Data	Uninformative	Text reports "occasional" focal areas of hepatic necrosis at the high dose; incidence values, timing, or statement of significance were not included. These results cannot be independently varified.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation

HERO ID: 200427 Table: 5 of 5

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**Study Citation:** Klaunig, J.E., Ruch, R.J., Pereira, M.A. (1986). Carcinogenicity of chlorinated methane and ethane compounds administered in drinking water to mice.

Environmental Health Perspectives 69:89-95.

Hepatic/Liver Health

**Outcome(s):** 

**Reported Health** Non-cancer lesions; liver weights

Effect(s):

**Duration:** Chronic (>91 days) 52 wks (24 wk interim sacrifice) - Cancer bioassay

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200427

Domain Metric Rating Comments

**Overall Quality Determination** Uninformative Study Citation: Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.

Banbury Report 5:3-29.

**Health** Mortality

**Outcome(s):** 

**Reported Health** Survival

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94773

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (CASRN 107-06-2).
	Metric 2:	Test Substance Source	High	The test substance was obtained from Montedison. Batch/lot number were not provided, but was analytically verified.
	Metric 3:	Test Substance Purity	High	Test substance was reported to be 99.82% pure.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Two negative control groups were included, an untreated group (maintained in a separate room) and chamber control.
	Metric 5:	Positive Controls	N/A	Not applicable for this study
	Metric 6:	Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Storage of test substance was not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	Low	Details of exposure administration are insufficiently reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Actual concentrations were not reported; the chamber concentration was controlled by continuous gas chromatography.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose was appropriate.
	Metric 12:	Exposure Route and Method	Low	Very minimal details about the methods for inhalation exposure administration were reported, resulting in uncertainty about the true exposure parameters. There are no details on inhalation exposure chamber/methodology (i.e., chamber airflow/volume, vaporization method, air changes, flow rate).
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were partially reported (humidity and light cycle were not).
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was appropriate (90/sex/group).

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Study Citation: Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.

Banbury Report 5:3-29.

Health

Mortality

Outcome(s):

**Reported Health** 

Survival

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94773

Domain		Metric	Rating	Comments
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Outcomes assessment methodology addressed the intended outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding execution of study protocol were limited.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate
	Metric 19:	Blinding of Assessors	N/A	Not necessary.
	Metric 20:	Negative Control Response	High	Negative control group response was appropriate.
Domain 6: Confoundi	ng / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Study did not report adequate information to determine presence of confounding variables; respiratory rate was not reported. Test animals lived until spontaneous death, which may affect health outcomes.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	High	Survival was adequately reported.

# **Overall Quality Determination**

## Medium

<b>Study Citation:</b>	Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.
	Banbury Report 5:3-29.

Health Outcome(s): Reported Health

Effect(s):

**Duration:** 

Neurological/Behavioral; Ocular/Sensory; Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Gastrointestinal; Immune/Hematological; Endocrine (Endocrine); Adipose (Adipose); Reproductive/Developmental;

Neurological/Behavioral: Histology on brain; Ocular/Sensory: Histology on zyblam gland and retrobulbar gland; Lung/Respiratory: Histology on diaphragm and lungs; Hepatic/Liver: Histology on liver; Renal/Kidney: Histology on kidney and bladder; Gastrointestinal: Histology on stomach, intestines, tongue and salivary gland; Immune/Hematological: Histology on spleen, lymph nodes, and thymus; Endocrine (Endocrine): Histology on pancreas; Adipose (Adipose): intrascapular brown fat; Reproductive/Developmental: Histology on gonads;

Chronic (>91 days) 78 weeks- rats

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as ethylene dichloride (CASRN 107-06-2).
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from Montedison. Batch/lot number were not provided, but was analytically verified.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was reported to be 99.82% pure.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Two negative control groups were included, an untreated group (maintained in a separate room) and chamber control.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not applicable for this study
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Study does not report how animals were allocated.
Domain 3: Exposure C	haracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Storage of test substance was not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	Low	All Outcomes: Details of exposure administration are insufficiently reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were not reported; the chamber concentration was controlled by continuous gas chromatography.
	Metric 10:	Exposure Frequency and Duration	High	Neurological/Behavioral: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 24 months (rats) or 18 months (mice).; Ocular/Sensory: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Lung/Respiratory: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Hepatic/Liver: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Renal/Kidney: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Gastrointestinal: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Immune/Hematological: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Endocrine (Endocrine): The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Reproductive/Developmental: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Reproductive/Developmental: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.; Reproductive/Developmental: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose was appropriate.

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Study Citation:	Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice. Banbury Report 5:3-29.							
Health		Neurological/Behavioral; Ocular/Sensory; Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Gastrointestinal; Immune/Hematological; Endocrine (En-						
Outcome(s):	docrine); Adipose (Adipose); Reproductive/Developmental;							
Reported Health	Neurologica	l/Behavioral: Histology on brain; Ocular/Se	ensory: Histolo	gy on zyblam gland and retrobulbar gland; Lung/Respiratory: Histology on di				
Effect(s):	aphragm and lungs; Hepatic/Liver: Histology on liver; Renal/Kidney: Histology on kidney and bladder; Gastrointestinal: Histology on stomach							
				een, lymph nodes, and thymus; Endocrine (Endocrine): Histology on pancreas				
<b>5</b>		lipose): intrascapular brown fat; Reproductive	e/Development	al: Histology on gonads;				
Duration:	•	of days) 78 weeks- rats						
Chemical:	1,1-Dichlord	bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	94773							
Domain		Metric	Rating	Comments				
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Very minimal details about the methods for inhalation exposure administration was a state of the state of th				
				istration were reported, resulting in uncertainty about the true exposure parameters. There are no details on inhalation exposure chamber/methodology (i.e., chamber air-				
				flow/volume, vaporization method, air changes, flow rate).				
				•				
Domain 4: Test Anin								
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Starting body weights were not reported.				
	Metric 14:	Adequacy and Consistency of Animal	Medium	All Outcomes: Husbandry conditions were partially reported (humidity and light cycle				
	M 15	Husbandry Conditions	N. 1.	were not).				
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was appropriate (90/sex/group).				
Domain 5: Outcome	Assessment							
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcomes assessment methodology addressed the intended outcomes o				
			8	interest.				
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: Details regarding execution of study protocol were limited.				
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary.				
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control group response was appropriate.				
Domain 6: Confound	•		<b>T</b>					
	Metric 21:	Confounding Variables in Test Design	Low	All Outcomes: Study did not report adequate information to determine presence of confounding variables; respiratory rate was not reported. Test animals lived until spont				
		and Procedures		neous death, which may affect health outcomes.				
	Metric 22:	Health Outcomes Unrelated to	Medium	All Outcomes: There was no information either to support or dismiss the suggestion the				
		Exposure		there were differences among groups in animal attrition or health outcomes unrelated t				
		•		exposure.				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.				
	Metric 24:	Reporting of Data	Medium	All Outcomes: Outcomes with negative findings are reported as such in the text.				

HERO ID: 94773 Table: 3 of 6

1,1-Dichloroethane

Study Citation: Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.

Banbury Report 5:3-29. Cancer/Carcinogenesis

**Outcome(s):** 

Health

**Reported Health** 

Tumors

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94773

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (CASRN 107-06-2).
	Metric 2:	Test Substance Source	High	The test substance was obtained from Montedison. Batch/lot number were not provided, but was analytically verified.
	Metric 3:	Test Substance Purity	High	Test substance was reported to be 99.82% pure.
Domain 2: Test Desig	⊇n			
	Metric 4:	Negative and Vehicle Controls	High	Two negative control groups were included, an untreated group (maintained in a separate room) and chamber control.
	Metric 5:	Positive Controls	N/A	Not applicable for this study
	Metric 6:	Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
Domain 3: Exposure	Characterization			
p	Metric 7:	Preparation and Storage of Test Substance	Low	Storage of test substance was not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported.
	Metric 9:	Reporting of Doses/Concentrations	Low	Actual concentrations were not reported; the chamber concentration was controlled by continuous gas chromatography.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.
	Metric 11:	Number of Exposure Groups and	High	The number of exposure groups and dose was appropriate.
	Metric 12:	Dose/Concentration Spacing Exposure Route and Method	Low	Very minimal details about the methods for inhalation exposure administration were reported, resulting in uncertainty about the true exposure parameters. There are no details on inhalation exposure chamber/methodology (i.e., chamber airflow/volume, vaporization method, air changes, flow rate).
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were partially reported (humidity and light cycle were not).
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was appropriate (90/sex/group).

#### Domain 5: Outcome Assessment

### Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.

Banbury Report 5:3-29. Cancer/Carcinogenesis

Health
Outcome(s):

Jutcome(s):

Reported Health

Tumors

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94773

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Uninformative	Animals were allowed to spontaneous death. With age, prevalence of cancer increases and it therefore cannot be assumed that presence of cancer is due to treatment with the test chemical.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding execution of study protocol were limited.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate
	Metric 19:	Blinding of Assessors	N/A	Not necessary.
	Metric 20:	Negative Control Response	Medium	There were difference between the two negative control groups in regards to incidences of benign mammary tumors.
Domain 6: Confounding /	' Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Study did not report adequate information to determine presence of confounding variables; respiratory rate was not reported. Test animals lived until spontaneous death, which may affect health outcomes.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	High	Outcomes with negative findings are reported as such in the text and reported as incidence data in tables.

### **Overall Quality Determination**

### Uninformative

Study Citation: Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.

Banbury Report 5:3-29.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substar	ice			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (CASRN 107-06-2).
	Metric 2:	Test Substance Source	High	The test substance was obtained from Montedison. Batch/lot number were not provided, but was analytically verified.
	Metric 3:	Test Substance Purity	High	Test substance was reported to be 99.82% pure.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Low	The negative control group was maintained in a nearby room and were not sham treated
	Metric 5:	Positive Controls	N/A	Not applicable for this study
	Metric 6:	Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
Domain 3: Exposure Cl	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Storage of test substance was not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	Low	Details of exposure administration are insufficiently reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Actual concentrations were not reported; the chamber concentration was controlled by continuous gas chromatography.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose was appropriate.
	Metric 12:	Exposure Route and Method	Low	Very minimal details about the methods for inhalation exposure administration were reported, resulting in uncertainty about the true exposure parameters. There are no details on inhalation exposure chamber/methodology (i.e., chamber airflow/volume, vaporization method, air changes, flow rate).
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were partially reported (humidity and light cycle were not).
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was appropriate (90/sex/group in treated groups; control had 115 males, 134 females).
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	High	Outcomes assessment methodology addressed the intended outcomes of interest.
		Continu	ued on next pa	ge

HERO ID: 94773 Table: 4 of 6

### ... continued from previous page

Study Citation: Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.

Banbury Report 5:3-29.

Health

Mortality

Outcome(s):

Reported Health

Survival

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks- mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94773

Domain	Metric	Rating	Comments
Metric	: 17: Consistency of Outcome Assessment	Medium	Details regarding execution of study protocol were limited.
Metric	: 18: Sampling Adequacy	High	Sampling was adequate
Metric	e 19: Blinding of Assessors	N/A	Not necessary.
Metric	20: Negative Control Response	High	Negative control group response was appropriate.
Domain 6: Confounding / Varial Metric	21: Confounding Variables in Test Design and Procedures	Low	Study did not report adequate information to determine presence of confounding variables; respiratory rate was not reported. Test animals lived until spontaneous death, which may affect health outcomes.
Metrio	22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Metric	23: Data Presentation and Analysis	High	Statistical analysis was appropriate.
Metric	24: Reporting of Data	High	Survival was adequately reported.

## **Overall Quality Determination**

### Medium

<b>Study Citation:</b>	Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.
	Banbury Report 5:3-29.
Health	Neurological/Behavioral; Ocular/Sensory; Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Gastrointestinal; Immune/Hematological; Endocrine (En-
Outcome(s):	docrine); Adipose (Adipose); Reproductive/Developmental;
Reported Health	Neurological/Behavioral: Histology on brain; Ocular/Sensory: Histology on zyblam gland and retrobulbar gland; Lung/Respiratory: Histology on di-
Effect(s):	aphragm and lungs; Hepatic/Liver: Histology on liver; Renal/Kidney: Histology on kidney and bladder; Gastrointestinal: Histology on stomach, intestines,
	tongue and salivary gland; Immune/Hematological: Histology on spleen, lymph nodes, and thymus; Endocrine (Endocrine): Histology on pancreas;
	Adipose (Adipose): intrascapular brown fat; Reproductive/Developmental: Histology on gonads;
Duration	Chronic (501 days) 78 weeks, mice

**Duration:** Chronic (>91 days) 78 weeks- mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94773

HERO ID.	77113			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as ethylene dichloride (CASRN 107-06-2)
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from Montedison. Batch/lot number were not provided, but was analytically verified.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was reported to be 99.82% pure.
Domain 2: Test Design				
S	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: The negative control group was maintained in a nearby room and were not sham treated.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not applicable for this study
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Study does not report how animals were allocated.
Domain 3: Exposure Ch	naracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Storage of test substance was not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure	Low	All Outcomes: Details of exposure administration are insufficiently reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were not reported; the chamber concentration was controlled by continuous gas chromatography.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 24 months (rats) or 18 months (mice).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose was appropriate.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Very minimal details about the methods for inhalation exposure administration were reported, resulting in uncertainty about the true exposure parameters. There are no details on inhalation exposure chamber/methodology (i.e., chamber airflow/volume, vaporization method, air changes, flow rate).
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Husbandry conditions were partially reported (humidity and light cycle were not).
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was appropriate (90/sex/group in treated groups; control had 115 males, 134 females).

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Study Citation:	Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice Banbury Report 5:3-29.							
Health			atory; Hepatic/L	iver; Renal/Kidney; Gastrointestinal; Immune/Hematological; Endocrine (En-				
Outcome(s):	_	ipose (Adipose); Reproductive/Developmen						
Reported Health	Neurological/Behavioral: Histology on brain; Ocular/Sensory: Histology on zyblam gland and retrobulbar gland; Lung/Respiratory: Histology on di-							
Effect(s):	tongue and	aphragm and lungs; Hepatic/Liver: Histology on liver; Renal/Kidney: Histology on kidney and bladder; Gastrointestinal: Histology on stomach, intestines, tongue and salivary gland; Immune/Hematological: Histology on spleen, lymph nodes, and thymus; Endocrine (Endocrine): Histology on pancreas;						
Duration:		Adipose (Adipose): intrascapular brown fat; Reproductive/Developmental: Histology on gonads; Chronic (>91 days) 78 weeks- mice						
Chemical:	•	bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	94773	ediane isomer. 1,2 Diemoroediane						
Domain		Metric	Rating	Comments				
Domain 5: Outcome A	Assessment Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcomes assessment methodology addressed the intended outcomes of				
	Metric 17:	Consistency of Outcome Assessment	Medium	interest.				
	Metric 17.	Sampling Adequacy		All Outcomes: Details regarding execution of study protocol were limited.  All Outcomes: Sampling was adequate				
	Metric 19:	Blinding of Assessors	High N/A	All Outcomes: Not necessary.				
	Metric 20:	•		•				
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control group response was appropriate.				
Domain 6: Confoundi	ng / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Study did not report adequate information to determine presence of confounding variables; respiratory rate was not reported. Test animals lived until spontaneous death, which may affect health outcomes.				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion the there were differences among groups in animal attrition or health outcomes unrelated to exposure.				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.				
	Metric 24:	Reporting of Data	Medium	All Outcomes: Outcomes with negative findings are reported as such in the text.				

HERO ID: 94773 Table: 6 of 6

Study Citation: Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.

Banbury Report 5:3-29. Cancer/Carcinogenesis

**Health Outcome(s):** 

Reported Health

Tumors

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks- mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94773

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nnce			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (CASRN 107-06-2).
	Metric 2:	Test Substance Source	High	The test substance was obtained from Montedison. Batch/lot number were not provided, but was analytically verified.
	Metric 3:	Test Substance Purity	High	Test substance was reported to be 99.82% pure.
Domain 2: Test Design	n			
	Metric 4:	Negative and Vehicle Controls	Low	The negative control group was maintained in a nearby room and were not sham treated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study
	Metric 6:	Randomized Allocation of Animals	Low	Study does not report how animals were allocated.
Domain 3: Exposure (	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Storage of test substance was not adequately described given the volatility of the test substance.
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported.
	Metric 9:	Reporting of Doses/Concentrations	Low	Actual concentrations were not reported; the chamber concentration was controlled by continuous gas chromatography.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate (7 hrs/day, 5 x/week for 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose was appropriate.
	Metric 12:	Exposure Route and Method	Low	Very minimal details about the methods for inhalation exposure administration were reported, resulting in uncertainty about the true exposure parameters. There are no details on inhalation exposure chamber/methodology (i.e., chamber airflow/volume, vaporization method, air changes, flow rate).
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were partially reported (humidity and light cycle were not).
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was appropriate (90/sex/group in treated groups; control had 115 males, 134 females).

#### Domain 5: Outcome Assessment

HERO ID: 94773 Table: 6 of 6

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**Study Citation:** Maltoni, C., Valgimigli, L., Scarnato, C. (1980). Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice.

Banbury Report 5:3-29. Cancer/Carcinogenesis

Health **Outcome(s):** 

**Reported Health** Tumors

Effect(s): **Duration:** 

Chronic (>91 days) 78 weeks- mice

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94773

Domain	Metric	Rating	Comments
Metric	e 16: Outcome Assessment Methodology	Uninformative	Animals were allowed to spontaneous death. With age, prevalence of cancer increases and it therefore cannot be assumed that presence of cancer is due to treatment with the test chemical.
Metric	217: Consistency of Outcome Assessment	Medium	Details regarding execution of study protocol were limited.
Metric	18: Sampling Adequacy	High	Sampling was adequate
Metric	19: Blinding of Assessors	N/A	Not necessary.
Metric	20: Negative Control Response	High	Negative control group response was appropriate.
Domain 6: Confounding / Varial Metric	21: Confounding Variables in Test Design and Procedures	Low	Study did not report adequate information to determine presence of confounding variables; respiratory rate was not reported. Test animals lived until spontaneous death, which may affect health outcomes.
Metric	22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
Metric	23: Data Presentation and Analysis	High	Statistical analysis was appropriate.
Metric	24: Reporting of Data	High	Outcomes with negative findings are reported as such in the text and reported as incidence data in tables.

# **Overall Quality Determination**

### Uninformative

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Body weights; body length

Effect(s):

**Duration:** Chronic (>91 days) 6 months; dogs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified definitively using standard nomenclature; CASRN was not provided.
Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
Metric 5:	Positive Controls	N/A	Not necessary for the study type
Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Characterization	n		
Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group (per chemical). Two chamber sizes were used; it is unclear which chamber size the air-only controls were in. However, the text indicates that all chambers had an equivalent rate of air change.
Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
Metric 10	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months on alternate days (75 days total); this frequency is less than guideline recommendations.
Metric 11	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for a chronic repeat exposure, this is less than guide- line recommendations and precludes the ability to evaluate a dose-response.
Metric 12:		Low	A whole-body dynamic air chamber was used for an inhalation study, the airflow rate (only reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Low	Species, sex, and age were reported. Mongrel dogs were used, which makes comparisons between the control and exposure groups difficult. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
Metric 14	Adequacy and Consistency of Animal Husbandry Conditions	Low	Insufficient information on animal husbandry conditions was reported (only the type of food was provided)

Human Health Hazard Animal Toxicology Evaluation HERO ID: 1973131 Table: 1 of 6

### ... continued from previous page

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weights; body length

Effect(s):

**Duration:** Chronic (>91 days) 6 months; dogs

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	Only a single male dog/group was used; the low number decreases the ability to characterize or observe a toxic effect.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	It was reported that weights were followed weekly.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of outcome assessment were not clearly reported. However, control and exposed dogs were evaluated after the same duration of exposure.
	Metric 18:	Sampling Adequacy	Low	Single animals were used for all endpoints.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Medium	The study authors did not indicate whether or not the control dog responses were unexpected.
Domain 6: Confoundin	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures.  Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis could not be performed due to an n of 1
	Metric 24:	Reporting of Data	High	Growth results were displayed graphically and were appropriate given the limitations in sample size. Body weights and pathology results were adequately reported.

## **Overall Quality Determination**

### Medium

HERO ID: 1973131 Table: 2 of 6

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

Survival

**Effect(s):** 

**Duration:** Chronic (>91 days) 6 months; dogs

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID: 1973131

HERO ID:	19/3131			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively using standard nomenclature; CASRN was not provided.
	Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Ch	naracterization			
-	Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group (per chemical). Two chamber sizes were used; it is unclear which chamber size the air-only controls were in. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months on alternate days (75 days total); this frequency is less than guideline recommendations.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for a chronic repeat exposure, this is less than guide- line recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Low	A whole-body dynamic air chamber was used for an inhalation study, the airflow rate (only reported to be "comfortable") and the rate of air change were not reported.
Domain 4: Test Animals				
Domain 4: Test Animais	Metric 13:	Test Animal Characteristics	Low	Species, sex, and age were reported. Mongrel dogs were used, which makes comparisons between the control and exposure groups difficult. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Insufficient information on animal husbandry conditions were reported (type of food was reported)
	Metric 15:	Number of Animals per Group	Low	Only a single male dog/group was used; this is considered to be low, but may be considered acceptable for dogs

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		contin	ued from p	revious page				
Study Citation: Health Outcome(s):	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons. Mortality							
Reported Health	Survival							
Effect(s):	Survivar							
Duration:	Chronic (>91 days) 6 months; dogs							
Chemical:	*	pethane- Isomer: 1,2-Dichloroethane						
HERO ID:	1973131	reducire 150mer. 1,2 Bremoroediane						
Domain		Metric	Rating	Comments				
Domain 5: Outcome	A accomment							
Domain 3: Outcome 2	Metric 16:	Outcome Assessment Methodology	Low	Beyond a list of what outcomes were evaluated, minimal details of the methods of outcome assessment were described. The frequency of animal observation was not reported.				
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of outcome assessment were not clearly reported. However, control and exposed dogs were evaluated after the same duration of exposure.				
	Metric 18:	Sampling Adequacy	Low	All animals were observed for mortality.				
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated				
	Metric 20:	Negative Control Response	High	Results for the control dog were as expected (no death)				
Domain 6: Confound	ing / Variable Co	ntrol						
Domain o. Comound	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.				
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis could not be performed due to an n of 1				
	Metric 24:	Reporting of Data	Low	Results were reported in the text as a negative outcome (no mortalities)				
Overall Qual	lity Deterr	nination	Low					

Study Citation: Health Outcome(s): Reported Health Effect(s):  Duration: Chemical: HERO ID:	Hepatic/Liv Reproductiv Hepatic/Liv Lung/Respir docrine (thy Adrenal): To Chronic (>9	re/Developmental (Endocrine (thyroid, parath) er: Live weights, histopathology; Renal/ ratory: Histopathology; Immune/Hematologic	iratory; Immun yroid, Pancreas 'Kidney: Kid cal: Blood cell	e/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively using standard nomenclature; CASRN was not provided.
	Metric 2:	Test Substance Source	Low	All Outcomes: A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	All Outcomes: Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animals were "distributed by randomization"; the method of randomization was not indicated.
Damain 2. Evragues Ch.				
Domain 3: Exposure Cha	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: The study consisted of only a single exposure group (per chemical). Two chamber sizes were used; it is unclear which chamber size the air-only controls were in. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reported.
	Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: Reported as 7hrs/day for 6 months on alternate days (75 days total); this frequency is less than guideline recommendations.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: A whole-body dynamic air chamber was used for an inhalation study, the airflow rate (only reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Species, sex, and age were reported. Mongrel dogs were used, which makes comparisons between the control and exposure groups difficult. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.

HERO ID: 1973131 Table: 3 of 6

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Study Citation:

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health Hepatic/Liver; Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);

Reported Health Effect(s):

Reported Health Hepatic/Liver: Live weights, histopathology; Renal/Kidney: Kidney weights and histopathology; serum BUN; Cardiovascular: Histology; Lung/Respiratory: Histopathology; Immune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Adrenal histopathology; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas,

Adrenal): Testis histopathology;

**Duration:** Chronic (>91 days) 6 months; dogs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1973131

Domain	Metric	Rating	Comments
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Insufficient information on animal husbandry conditions was reported (only the type of food was provided)
Metric 15:	Number of Animals per Group	Low	All Outcomes: Only a single male dog/group was used; the low number decreases the ability to characterize or observe a toxic effect.

#### Domain 5: Outcome Assessment

Metric 16: Outcome Assessment Methodology Medium

Hepatic/Liver: The outcome assessment methodology was appropriate, (e.g., organ weights, histopathology, serum chemistry/hematology), however, some details were limited (e.g., for histology, no information regarding the number of slides or staining used). Methods for the thymol-barbital test was cited to another publication. Limited to no details of methods of the brom sulfalein retention test were provided.; Renal/Kidney: The outcome assessment methodology was appropriate, (e.g., organ weights, histopathology, serum chemistry/hematology), however, some details were limited (e.g., for histology, no information regarding the number of slides or staining used).; Cardiovascular: The outcome assessment methodology was appropriate, (e.g., organ weights, histopathology, serum chemistry/hematology), however, some details were limited (e.g., for histology, no information regarding the number of slides or staining used).; Lung/Respiratory: Only histology for this endpoint was performed; information regarding the number of slides or staining used.; Immune/Hematological: The outcome assessment methodology was appropriate, (e.g., organ weights, histopathology, serum chemistry/hematology), however, some details were limited (e.g., for histology, no information regarding the number of slides or staining used).; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Only histology for this endpoint was performed; information regarding the number of slides or staining used.; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Only histology for this endpoint was performed; information regarding the number of slides or staining used.

### ... continued from previous page

<b>Study Citation:</b>	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health	Hepatic/Liver; Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Outcome(s):	Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health	Hepatic/Liver: Live weights, histopathology; Renal/Kidney: Kidney weights and histopathology; serum BUN; Cardiovascular: Histology;
Effect(s):	Lung/Respiratory: Histopathology; Immune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Endocrine (En-
	docrine (thyroid, parathyroid, Pancreas, Adrenal): Adrenal histopathology; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas,
	Adrenal): Testis histopathology;
<b>Duration:</b>	Chronic (>91 days) 6 months; dogs

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

HERO ID:	1973131	· · · · · · · · · · · · · · · · · · ·		
Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Medium	Hepatic/Liver: Details of outcome assessment were not clearly reported for some outcomes (e.g., bromsulfalein, although dates of the collections between exposed and control dogs were equivalent, and thymol-barbital test). For other relevant outcomes, data for control and exposed dogs were consistently collected.; Renal/Kidney: Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Cardiovascular: Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Lung/Respiratory: Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Immune/Hematological: Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Details of outcome assessment were not clearly reported, but collections dates were provided in data tables for some outcomes and data for control and exposed dogs were consistently collected.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Single animals were used for all endpoints.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Medium	All Outcomes: The study authors did not indicate whether or not the control dog responses were unexpected.
Domain 6: Confoundir	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
		Contin	ued on next pa	nge

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Study Citation:

Health
Outcome(s):
Reported Health
Effect(s):

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Hepatic/Liver; Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);

Reported Health
Effect(s):

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Hepatic/Liver; Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (Endocrine));

Hepatic/Liver: Live weights, histopathology; Renal/Kidney: Kidney weights and histopathology; serum BUN; Cardiovascular: Histology;

Lung/Respiratory: Histopathology; Immune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Adrenal histopathology; Reproductive/Developmental (Endocrine (thyroid, Pancreas, Adrenal): Adrenal histopathology; Reproductive/Developmental (Endocrine (thyroid, Pancreas, Adrenal): Adrenal histopa

docrine (thyroid, parathyroid, Pancreas, Adrenal): Adrenal histopathology; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Industrial): Testis histopathology;

**Duration:** Chronic (>91 days) 6 months; dogs

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	N/A	Hepatic/Liver: Statistical analysis was not possible for most endpoints (n=1), however, the study Authors applied statistical analysis in some cases (e.g., means of urea nitrogen and phosphate units derived from multiple collection times were compared to controls by the "t" test). Although this allows for some comparison even with use of single animals, it could dilute or mask changes occurring after longer exposure times and therefore may not be appropriate.; Renal/Kidney: Statistical analysis was not possible for most endpoints (n=1); Cardiovascular: Statistical analysis was not possible for most endpoints (n=1); Lung/Respiratory: Statistical analysis was not possible for most endpoints (n=1); Immune/Hematological: Statistical analysis was not possible for most endpoints (n=1); Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Statistical analysis was not possible for most endpoints (n=1); Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal): Statistical analysis was not possible for most endpoints (n=1)
	Metric 24:	Reporting of Data	High	All Outcomes: Individual animal data were provided for all endpoints.

### **Overall Quality Determination**

### **Medium**

HERO ID: 1973131 Table: 4 of 6

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Mortality

**Outcome(s):** 

Reported Health

Survival

Effect(s):

**Duration:** Chronic (>91 days) 6 months; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Identified as ethylene dichloride (1,2-dichloroethane); CASRN not provided
	Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
Bomain 2. Test Besign	Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure C	haracterization			
rr	Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group. Two chamber sizes were used, and it is unclear if the air-only controls were in the same chamber size. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months; the frequency of exposure was not clearly stated. The text indicated that 75 exposure days had been completed. 75, 7-hr exposures over a span of 6 months (24 weeks) would be ~2 exposure days/week?
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for chronic repeat exposure, this is less than guidelin recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Medium	A whole body dynamic air chamber was used for an inhalation study, the air flow rate (reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animal	ls			
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and age were reported. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Information included # animals/cage (n=6), food and water. No other animal husbandry details were provided. It is unclear if housing conditions were appropriate given problems with animal infections,
	Metric 15:	Number of Animals per Group	Low	The number of animals (12/sex) is lower than guideline recommendations for a chronic study in rats

HERO ID: 1973131 Table: 4 of 6

## ... continued from previous page

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Mortality

**Outcome(s):** 

**Reported Health** 

Survival

Effect(s):

**Duration:** Chronic (>91 days) 6 months; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1973131

Domain		Metric	Rating	Comments
Domain 5: Outcom	e Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	Beyond a list of what outcomes were evaluated, minimal details of the methods of outcome assessment were described. The frequency of animal observation was not reported.
	Metric 17:	Consistency of Outcome Assessment	Low	Details of outcome assessment were not clearly reported.
	Metric 18:	Sampling Adequacy	High	All animals were observed for mortality
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Uninformative	The mortality rate of the control group was reported to be 57% (due to the presence of lung infections)
Domain 6: Confour	nding / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	A significant number of animals died in all groups to due apparent lung infections unrelated to exposure. This significantly impacted the usefulness of this study.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was likely not performed due to the significant deaths resulting from lung infections in all groups (including the controls)
	Metric 24:	Reporting of Data	Medium	No direct comparisons were made with controls, but mortality rates for both controls and the exposed group was reported.

# **Overall Quality Determination**

## Uninformative

HERO ID: 1973131 Table: 5 of 6

**Study Citation:** 

Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health

Kidney weights and histopathology; serum BUN

**Effect(s):** 

**Duration:** Chronic (>91 days) 6 months; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1973131

HERO ID.	1973131			
Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	Identified as ethylene dichloride (1,2-dichloroethane); CASRN not provided
	Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided.
	Metric 3:	Test Substance Purity	Low	Reported to be commercial grade, but purity was not provided.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	Animals were "distributed by randomization"; the method of randomization was not indicated.
Domain 3: Exposure Cl	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The study consisted of only a single exposure group. Two chamber sizes were used, and it is unclear if the air-only controls were in the same chamber size. However, the text indicates that all chambers had an equivalent rate of air change.
	Metric 9:	Reporting of Doses/Concentrations	High	Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.
	Metric 10:	Exposure Frequency and Duration	Low	Reported as 7hrs/day for 6 months; the frequency of exposure was not clearly stated. The text indicated that 75 exposure days had been completed. 75, 7-hr exposures over a span of 6 months (24 weeks) would be ~2 exposure days/week?
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	A single exposure group was used for chronic repeat exposure, this is less than guidelin recommendations and precludes the ability to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	Medium	A whole body dynamic air chamber was used for an inhalation study, the air flow rate (reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and age were reported. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Information included # animals/cage (n=6), food and water. No other animal husbandry details were provided. It is unclear if housing conditions were appropriate given problems with animal infections,
	Metric 15:	Number of Animals per Group	Low	The number of animals (12/sex) is lower than guideline recommendations for a chronic study in rats

# Human Health Hazard Animal Toxicology Evaluation

## ... continued from previous page

**Study Citation:** Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

Health

Renal/Kidney

**Outcome(s):** 

Reported Health

Kidney weights and histopathology; serum BUN

Effect(s):

**Duration:** Chronic (>91 days) 6 months; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 197313

HERO ID:	19/3131			
Domain		Metric	Rating	Comments
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Outcome assessment methods were appropriate, but were poorly described (e.g., no details on tissue collection, histology methods used, etc.,)
	Metric 17:	Consistency of Outcome Assessment	Low	Details of outcome assessment were not clearly reported (i.e, it is unclear what animals were included in the dataset, and whether the animals added after 30 days were pooled with the original group of animals that survived, as was indicated for some other endpoints).
	Metric 18:	Sampling Adequacy	Low	The number of animals contributing to the measurements are not reported.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the endpoint evaluated
	Metric 20:	Negative Control Response	Uninformative	57% of control animals died; Roughly 50% of control animals evaluated had major pathology of the kidney (25%), liver (30%), or lung (29%).
Domain 6: Confound	ding / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report confounding variables related to test design and procedures.  Respiratory rates were not monitored
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	Animals from all groups were reported to have a virus, or pleurpneumonia like organism/infection. This significantly affected the reliability of this study
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was not performed; it is presumed this is due to the poor health of the control animals. Statistical analysis was performed for organ weights; however, the methods were not adequately described.
	Metric 24:	Reporting of Data	Low	Summary tables did not include measures of variance and the summary table for pathol ogy data was ambiguously reported. Samples were described as "sets of tissues examined" and "sets with major pathology" without distinguishing between males and females, or if data were from animals exposed for 45 days (e.g., animals added midstudy), or 75 days. However, individual animal data were adequately presented in tables at the end of the study.

## **Overall Quality Determination**

## Uninformative

HERO ID: 1973131 Table: 6 of 6

**Study Citation:** Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

**Health** Reproductive/Developmental; Lung/Respiratory; Hepatic/Liver; Immune/Hematological; Cardiovascular; Lung/Respiratory; Endocrine;

**Outcome(s):** 

Reported Health Reproductive/Developmental: Testis histopathology; Lung/Respiratory: Histopathology; Hepatic/Liver: Live weights, histopathology; Immune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Cardiovascular: Histology; Lung/Respiratory:

Histopathology; Endocrine: Adrenal histopathology;

**Duration:** Chronic (>91 days) 6 months; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1973131

Domain	Metric	Rating	Comments		
Domain 1: Test Substance					
Metric 1:	Test Substance Identity	High	Reproductive/Developmental: Identified as ethylene dichloride (1,2-dichloroethane); CASRN not provided; Lung/Respiratory: Identified as ethylene dichloride (1,2-dichloroethane); CASRN not provided; Hepatic/Liver: Identified as ethylene dichloride (1,2-dichloroethane); CASRN not provided; Immune/Hematological: The test substance was identified definitively using standard nomenclature; CASRN was not provided.; Cardiovascular: The test substance was identified definitively using standard nomenclature; CASRN was not provided.; Lung/Respiratory: Identified as propylene dichloride (1,2-dichloropropane); CASRN not provided; Endocrine: The test substance was identified definitively using standard nomenclature; CASRN was not provided.		
Metric 2:	Test Substance Source	Low	All Outcomes: A commercial source was identified; batch and lot numbers were not provided.		
Metric 3:	Test Substance Purity	Low	All Outcomes: Reported to be commercial grade, but purity was not provided.		
Domain 2: Test Design					
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The document indicates there was an exposed control group; animals were exposed to the same conditions as exposed animals without the vapors.		
Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type		
Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Animals were "distributed by randomization"; the method of randomization was not indicated.		
Domain 3: Exposure Characterization	n				
Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: The study includes a limited description of the method of vapor generation, but storage of the test substance was not reported.		
Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: The study consisted of only a single exposure group. Two chamber sizes were used, and it is unclear if the air-only controls were in the same chamber size. However, the text indicates that all chambers had an equivalent rate of air change.		
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target and analytical vapor concentrations were reported. Vapor concentrations were monitored daily using a Zeiss interferometer. The sensitivity values for the interferometer based on thermal decomposition methods were reproted.		
Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: Reported as 7hrs/day for 6 months; the frequency of exposure was not clearly stated. The text indicated that 75 exposure days had been completed. 75, 7-hr exposures over a span of 6 months (24 weeks) would be ~2 exposure days/week?		

**Study Citation:** Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons. Health

Reproductive/Developmental; Lung/Respiratory; Hepatic/Liver; Immune/Hematological; Cardiovascular; Lung/Respiratory; Endocrine;

**Outcome(s):** 

**Reported Health** Reproductive/Developmental: Testis histopathology; Lung/Respiratory: Histopathology; Hepatic/Liver: Live weights, histopathology; Im-Effect(s): mune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Cardiovascular: Histology; Lung/Respiratory:

> Histopathology; Endocrine: Adrenal histopathology; Chronic (>91 days) 6 months; rats

**Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HEDA ID

HERO ID:	1973131			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Reproductive/Developmental: A single exposure group was used for chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Lung/Respiratory: A single exposure group was used for chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Hepatic/Liver: A single exposure group was used for chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Immune/Hematological: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Cardiovascular: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Lung/Respiratory: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Endocrine: A single exposure group was used for a chronic repeat exposure, this is less than guideline recommendations and precludes the ability to evaluate a dose-response.; Endocrine: A
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: A whole body dynamic air chamber was used for an inhalation study, the air flow rate (reported to be "comfortable") and rate of air change were not reported.
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Species, strain, sex, and age were reported. Initial body weights were not explicitly reported, but are indicated in a graph at 0 weeks of exposure.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Information included # animals/cage (n=6), food and water. No other animal husbandry details were provided. It is unclear if housing conditions were appropriate given problems with animal infections,
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals (12/sex) is lower than guideline recommendations for a chronic study in rats
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Outcome assessment methods were appropriate, but were poorly described (e.g., no details on tissue collection, histology methods used, etc.,)
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Details of outcome assessment were not clearly reported (i.e, it is unclear what animals were included in the dataset, and whether the animals added after 30 days were pooled with the original group of animals that survived, as was indicated for some other endpoints).
	Metric 18:	Sampling Adequacy	Low	All Outcomes: The number of animals contributing to the measurements are not reported.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the endpoint evaluated

**Study Citation:** Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.

**Health** Reproductive/Developmental; Lung/Respiratory; Hepatic/Liver; Immune/Hematological; Cardiovascular; Lung/Respiratory; Endocrine;

**Outcome(s):** 

Reported Health Effect(s):

Reproductive/Developmental: Testis histopathology; Lung/Respiratory: Histopathology; Hepatic/Liver: Live weights, histopathology; Immune/Hematological: Blood cell counts and hemoglobin determinations; Spleen histopathology; Cardiovascular: Histology; Lung/Respiratory:

HERO ID: 1973131 Table: 6 of 6

Histopathology; Endocrine: Adrenal histopathology;

**Duration:** Chronic (>91 days) 6 months; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 1973131

Domain	Metric	Rating	Comments
Metric	20: Negative Control Response	Uninformative	All Outcomes: 57% of control animals died; Roughly 50% of control animals evaluated had major pathology of the kidney (25%), liver (30%), or lung (29%).
Domain 6: Confounding / Variab	le Control		
Metric	21: Confounding Variables in Test Design and Procedures	Low	All Outcomes: The study did not report confounding variables related to test design and procedures. Respiratory rates were not monitored
Metric	22: Health Outcomes Unrelated to Exposure	Uninformative	All Outcomes: Animals from all groups were reported to have a virus, or pleurpneumonia like organism/infection. This significantly affected the reliability of this study
Metric		Low	All Outcomes: Statistical analysis was not performed; it is presumed this is due to the poor health of the control animals. Statistical analysis was performed for organ weights; however, the methods were not adequately described.
Metric	24: Reporting of Data	Medium	All Outcomes: Summary tables did not include measures of variance and the summary table for pathology data was ambiguously reported. Samples were described as "sets of tissues examined" and "sets with major pathology" without distinguishing between males and females, or if data were from animals exposed for 45 days (e.g., animals added mid-study), or 75 days. However, individual animal data were adequately presented in tables at the end of the study.

## **Overall Quality Determination**

## Uninformative

HERO ID: 200497 Table: 1 of 3

**Study Citation:** Nagano, K., Umeda, Y., Senoh, H., Gotoh, K., Arito, H., Yamamoto, S., Matsushima, T. (2006). Carcinogenicity and chronic toxicity in rats and mice exposed by inhalation to 1,2-dichloroethane for two years. Journal of Occupational Health 48(6):424-436.

Health Immune/Hematological; Nutritional/Metabolic;

**Outcome(s):** 

**Reported Health** Immune/Hematological: Hematology; Nutritional/Metabolic: Body weight and food intake;

Effect(s):

**Duration:** Chronic (>91 days) 2 years

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric		Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-Dichloroethane.
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was Wako Pure Chemical Industries, Ltd (Osaka, Japan). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of the test substance was greater than 99%.
Domain 2: Test Design				
· ·	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Appropriate negative controls were used (clean air).
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were divided by stratified randomization into 4 body weight matched groups.
Domain 3: Exposure Ch	naracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: There were deficiencies in preparation and storage conditions of test substances.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Target and measured concentrations were reported and appropriate.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration (2 years) were reported and appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose spacing were appropriate with the high dose based on subchronic toxicity study.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Whole body chambers were used with 12 +/-1 air changes/hour.
Domain 4: Test Animals	s			
	Metric 13:	Test Animal Characteristics	High	All Outcomes: All test animal characteristics were reported.
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were sufficiently reported.
		Husbandry Conditions	C	, , ,
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed per group were appropriate (50/sex/group).
Domain 5: Outcome As	gaggmant			
Domain J. Outcome As	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methodology were appropriate.
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: Details of outcomes assessment were limited.
		Contin	nued on nex	et page

HERO ID: 200497 Table: 1 of 3

#### ... continued from previous page

**Study Citation:** Nagano, K., Umeda, Y., Senoh, H., Gotoh, K., Arito, H., Yamamoto, S., Matsushima, T. (2006). Carcinogenicity and chronic toxicity in rats and mice

exposed by inhalation to 1,2-dichloroethane for two years. Journal of Occupational Health 48(6):424-436.

Health Immune/Hematological; Nutritional/Metabolic;

**Outcome(s):** 

**Reported Health** 

Immune/Hematological: Hematology; Nutritional/Metabolic: Body weight and food intake;

Effect(s):

Chronic (>91 days) 2 years **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200497

Domain	Metric	Rating	Comments
Metric 18:	Sampling Adequacy	High	All Outcomes: All 50 animals were evaluated.
Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were appropriate.
Domain 6: Confounding / Variable Co Metric 21:	ntrol Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.
Metric 24:	Reporting of Data	High	Immune/Hematological: Data was reported in text. No exposure-related changes in hematological or blood biochemical parameters were found in any DCE-exposed group of either sex of rats and mice.; Nutritional/Metabolic: Body weight were reported.

# **Overall Quality Determination**

# High

HERO ID: 200497 Table: 2 of 3

1,1-Dichloroethane

Study Citation: Nagano, K., Umeda, Y., Senoh, H., Gotoh, K., Arito, H., Yamamoto, S., Matsushima, T. (2006). Carcinogenicity and chronic toxicity in rats and mice

exposed by inhalation to 1,2-dichloroethane for two years. Journal of Occupational Health 48(6):424-436.

Health

Lung/Respiratory

**Outcome(s):** 

**Reported Health** 

Lung weight and histology

Effect(s):

**Duration:** Chronic (>91 days) 2 years

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200497

Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-Dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was Wako Pure Chemical Industries, Ltd (Osaka,
				Japan). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was greater than 99%.
Domain 2: Test Desi	gn			
	Metric 4:	Negative and Vehicle Controls	High	Appropriate negative controls were used (clean air).
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were divided by stratified randomization into 4 body weight matched groups.
Domain 3: Exposure	Characterization			
Domain of Emposure	Metric 7:	Preparation and Storage of Test	Low	There were deficiencies in preparation and storage conditions of test substances.
		Substance		
	Metric 8:	Consistency of Exposure	High	Exposure was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Target and measured concentrations were reported and appropriate.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration (2 years) were reported and appropriate.
	Metric 11:	Number of Exposure Groups and	High	The number of exposure groups and dose spacing were appropriate with the high dose
	Medic 11.	Dose/Concentration Spacing	mgn	based on subchronic toxicity study.
	Metric 12:	Exposure Route and Method	Medium	Whole body chambers were used with 12 +/-1 air changes/hour.
		*		
Domain 4: Test Anir		m	TT' 1	
	Metric 13:	Test Animal Characteristics	High	All test animal characteristics were reported.
	Metric 14:	Adequacy and Consistency of Animal	High	Husbandry conditions were sufficiently reported.
	Matria 15:	Husbandry Conditions	Madines	The mank of simple and a superior (50)
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed per group were appropriate (50/sex/group).
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology were appropriate.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of outcomes assessment were limited.
	Metric 18:	Sampling Adequacy	High	All 50 animals were evaluated.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	The negative control responses were appropriate.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 200497 Table: 2 of 3

#### ... continued from previous page

Study Citation: Nagano, K., Umeda, Y., Senoh, H., Gotoh, K., Arito, H., Yamamoto, S., Matsushima, T. (2006). Carcinogenicity and chronic toxicity in rats and mice

exposed by inhalation to 1,2-dichloroethane for two years. Journal of Occupational Health 48(6):424-436.

Health Lung/Respiratory

Outcome(s):

Reported Health

Lung weight and histology

**Effect(s):** 

**Duration:** Chronic (>91 days) 2 years

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200497

Domain	Metric		Rating	Comments
Domain 6: Confounding /	Variable Con	trol		
	Metric 21:	Confounding Variables in Test Design	Low	Test substance is a respiratory irritant therefore respiratory rate should be reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	Low	Data only reported for high dose group and control (female mice)

# Overall Quality Determination High

HERO ID: 200497 Table: 3 of 3

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Study Citation:	Nagano, K., Umeda, Y., Senoh, H., Gotoh, K., Arito, H., Yamamoto, S., Matsushima, T. (2006). Carcinogenicity and chronic toxicity in rats and mice
	exposed by inhalation to 1,2-dichloroethane for two years. Journal of Occupational Health 48(6):424-436.
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Health

Cancer/Carcinogenesis; Mortality;

**Outcome(s): Reported Health** 

Cancer/Carcinogenesis: Macroscopic and microscopic lesions were assessed.; Mortality: Mortality;

**Effect(s):** 

**Duration:** Chronic (>91 days) 2 years

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID.	200497			
Domain		Metric	Rating	Comments
Domain 1: Test Substar	ice			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-Dichloroethane.
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was Wako Pure Chemical Industries, Ltd (Osaka, Japan). Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of the test substance was greater than 99%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Appropriate negative controls were used (clean air).
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were divided by stratified randomization into 4 body weight matched groups.
Domain 3: Exposure Cl	naracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: There were deficiencies in preparation and storage conditions of test substances.
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	All Outcomes: Target and measured concentrations were reported and appropriate.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration (2 years) were reported and appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose spacing were appropriate with the high dose based on subchronic toxicity study.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Whole body chambers were used with 12 +/-1 air changes/hour.
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	High	All Outcomes: All test animal characteristics were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Husbandry conditions were sufficiently reported.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed per group were appropriate (50/sex/group).
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methodology were appropriate.
			Medium	All Outcomes: Details of outcomes assessment were limited.

HERO ID: 200497 Table: 3 of 3

#### ... continued from previous page

Study Citation: Nagano, K., Umeda, Y., Senoh, H., Gotoh, K., Arito, H., Yamamoto, S., Matsushima, T. (2006). Carcinogenicity and chronic toxicity in rats and mice

exposed by inhalation to 1,2-dichloroethane for two years. Journal of Occupational Health 48(6):424-436.

**Health** Cancer/Carcinogenesis; Mortality;

Outcome(s):

**Reported Health** 

Cancer/Carcinogenesis: Macroscopic and microscopic lesions were assessed.; Mortality: Mortality;

**Effect(s):** 

**Duration:** Chronic (>91 days) 2 years

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
	Metric 18:	Sampling Adequacy	High	Cancer/Carcinogenesis: The number of animals evaluated were reported.; Mortality: All 50 animals were evaluated.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were appropriate.
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be reported.
Domain 6: Confound	U		Low	All Outcomes: Test substance is a respiratory irritant therefore respiratory rate should be
	Metric 22:	Health Outcomes Unrelated to	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Exposure Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	Medium	Cancer/Carcinogenesis: Not all outcome data were reported, these minor uncertainties are unlikely to have a substantial impact on results (e.g. negative results are indicated in text).; Mortality: Not all outcome data were reported (e.g. age animals died)

Study Citation: Health NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Immune/Hematological

**Outcome(s):** 

**Reported Health** Histology

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks; Mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and $CASRN$ )
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and the identity was not analytically verified by the performing laboratory
	Metric 3:	Test Substance Purity	Medium	Reported as technical grade; no additional information provided.
D : 0 T : D :				
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	Allocation of test animals was not reported.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure Administration	High	Dosing administration was complicated (e.g., starting on week 36, intubation ceased for all treated animals for 1 week, followed by 4 weeks of dose administration. This pattern continued for the remainder of the dosing period), but treated and vehicle control groups were consistently treated in the same manner.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Gavage volumes not reported
	Metric 10:	Exposure Frequency and Duration	High	Animals were treated 5 days/week for 78 weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Doses and spacing were determined based on preliminary studies. However, no reasoning was provided for the change in doses throughout the study.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.

Study Citation: Health NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Immune/Hematological

**Outcome(s):** 

**Reported Health** 

Histology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

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Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	50/sex in the treatment groups (20/sex controls)
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The endpoint was consistently assessed across all groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate. In some cases, the number of animals/group evaluated differed due to exclusion of animals that died early, or missing or cannibalized, or partially autolyzed animals
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study result
	Metric 20:	Negative Control Response	Low	In males, the incidence of lesions in the spleen is very high (e.g. $> 30\%$ ) in the control group, making it difficult to detect an effect of treatment. Control responses in females were adequate.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Sufficient data were provided to conduct an independent statistical analysis.
	Metric 24:	Reporting of Data	High	Histology incidence data for this organ/system were adequately reported.

# **Overall Quality Determination**

# High

HERO ID: 5441108 Table: 2 of 11

Study Citation: Health Outcome(s): Reported Health Effect(s): Duration: Chemical: HERO ID:	Cardiovascu docrine); Cardiovascu (Endocrine): Chronic (>9	lar; Thyroid; Hepatic/Liver; Lung/Respirate lar: Histology; Thyroid: Histology; Hepati	ory; Skin/Co ic/Liver: His	nicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103. nnective Tissue; Endocrine (Endocrine); Gastrointestinal; Cancer/Carcinogenesis (Entology; Lung/Respiratory: Histology; Skin/Connective Tissue: Histology; Endocrine ty; Cancer/Carcinogenesis (Endocrine): Tumor formation;
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)
	Metric 2:	Test Substance Source	Low	All Outcomes: The test substance source was not reported and the identity was not analytically verified by the performing laboratory
	Metric 3:	Test Substance Purity	Medium	All Outcomes: Reported as technical grade; no additional information provided.
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Allocation of test animals was not reported.
Domain 3: Exposure Ch	naracterization Metric 7:	Preparation and Storage of Test	Low	All Outcomes: Information on preparation and storage was not reported and lack of
		Substance		details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure	Low	All Outcomes: Gavage volumes not reported
	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	All Outcomes: Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	High	Cardiovascular: Animals were treated 5 days/week for 78 weeks; Thyroid: Animals were treated 5 days/week for 78 weeks; Hepatic/Liver: Animals were treated 5 days/week for 78 weeks; Lung/Respiratory: Animals were treated 5 days/week for 78 weeks; Skin/Connective Tissue: Animals were treated 5 days/week for 78 weeks; Endocrine (Endocrine): Animals were treated 5 days/week for 78 weeks at survived, were dosed through 78 weeks.; Gastrointestinal: Animals were treated 5 days/week for 78 weeks; Cancer/Carcinogenesis (Endocrine): Animals were treated 5 days/week for 78 weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Doses and spacing were determined based on preliminary studies. However, no reasoning was provided for the change in doses throughout the study.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance

HERO ID: 5441108 Table: 2 of 11

## ... continued from previous page

Study Citation:				nicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.				
Health Outcome(s): Reported Health Effect(s): Duration: Chemical:	Cardiovascular; Thyroid; Hepatic/Liver; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine); Gastrointestinal; Cancer/Carcinogenesis (Endocrine); Cardiovascular: Histology; Thyroid: Histology; Hepatic/Liver: Histology; Lung/Respiratory: Histology; Skin/Connective Tissue: Histology; Endocrine (Endocrine): Adrenal, pituitary histology; Gastrointestinal: Histology; Cancer/Carcinogenesis (Endocrine): Tumor formation; Chronic (>91 days) 78 weeks; Mice							
HERO ID:	5441108	ethane- Isomer: 1,2-Dichloroethane						
Domain		Metric	Rating	Comments				
Domain 4: Test Animals								
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.				
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 50/sex in the treatment groups (20/sex controls)				
Domain 5: Outcome Ass	essment							
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.				
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The endpoint was consistently assessed across all groups.				
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate. In some cases, the number of animals/group evaluated differed due to exclusion of animals that died early, or missing or cannibalized, or partially autolyzed animals				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this study result				
	Metric 20:	Negative Control Response	High	Cardiovascular: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).; Thyroid: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).; Hepatic/Liver: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).; Lung/Respiratory: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).; Skin/Connective Tissue: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).; Endocrine (Endocrine): The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).; Gastrointestinal: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).; Cancer/Carcinogenesis (Endocrine): The incidence of tumors in male and female control mice was low.				

		···contin	ucu mom p	revious page
Study Citation: Health Outcome(s): Reported Health Effect(s): Duration: Chemical: HERO ID:	Cardiovascu docrine); Cardiovascu (Endocrine): Chronic (>9	lar; Thyroid; Hepatic/Liver; Lung/Respirate lar: Histology; Thyroid: Histology; Hepati	ory; Skin/Co c/Liver: His	nicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.  nnective Tissue; Endocrine (Endocrine); Gastrointestinal; Cancer/Carcinogenesis (Endocrine); Ung/Respiratory: Histology; Skin/Connective Tissue: Histology; Endocring; Cancer/Carcinogenesis (Endocrine): Tumor formation;
Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Cardiovascular: Sufficient data were provided to conduct an independent statistical analysis.; Thyroid: Sufficient data were provided to conduct an independent statistical analysis.; Hepatic/Liver: Sufficient data were provided to conduct an independent statistical analysis.; Lung/Respiratory: Sufficient data were provided to conduct an independent statistical analysis.; Skin/Connective Tissue: Sufficient data were provided to conduct an independent statistical analysis.; Endocrine (Endocrine): Sufficient data were provided to conduct an independent statistical analysis.; Gastrointestinal: Sufficient data were provided to conduct an independent statistical analysis.; Cancer/Carcinogenesis (Endocrine): A detailed description of statistical analyses was provided and was adequate.
	Metric 24:	Reporting of Data	High	Cardiovascular: Histology incidence data for this organ/system were adequately reported.; Thyroid: Histology incidence data for this organ/system were adequately reported.; Hepatic/Liver: Histology incidence data for this organ/system were adequately reported.; Lung/Respiratory: Histology incidence data for this organ/system were adequately reported.; Skin/Connective Tissue: Histology incidence data for this organ/system were adequately reported.; Endocrine (Endocrine): Histology incidence data for this organ/system were adequately reported.; Gastrointestinal: Histology incidence data for this organ/system were adequately reported.; Cancer/Carcinogenesis (Endocrine): Tumor incidence data were adequately reported.

## **Overall Quality Determination**

# High

Study Citation: NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Bodyweight, food consumption

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	5441108			
Domain		Metric	Rating	Comments
Domain 1: Test Substance	e			
	Metric 1:	Test Substance Identity	High	The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and the identity was not analytically verified by the performing laboratory
	Metric 3:	Test Substance Purity	Medium	Reported as technical grade; no additional information provided.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	Both vehicle (corn oil) and untreated control groups were included. *Note, the untreate controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	Allocation of test animals was not reported.
Domain 3: Exposure Cha	practerization			
Boniani 3. Exposure Che	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure	Low	Gavage volumes not reported
	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	High	Animals were treated 5 days/week for 78 weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Doses and spacing were determined based on preliminary studies. However, no reasoning was provided for the change in doses throughout the study.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103. Nutritional/Metabolic

Health

Outcome(s):

Reported Health Bodyweight, food consumption

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

neko ib.	3111100			
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	50/sex in the treatment groups (20/sex controls)
Domain 5: Outcome	Assessment			
Bonian 3. Gucone	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The endpoint was consistently assessed across all groups
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study result
	Metric 20:	Negative Control Response	High	There is no indication in the data provided that control responses were not as expected.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analyses of body weight data were not performed. Data could potentially be extracted from growth curves, but the number of animals for each data point is not reported.
	Metric 24:	Reporting of Data	Low	Bodyweight data were reported graphically as growth curves in the absence of measures of variance. No statistical results were reported, and the text indicates that Fluctuations in the growth curves may be due to mortality; as the size of the group diminishes, the mean body weight may be subject to wide variations. Food consumption was supposedly monitored but results were not reported.

# **Overall Quality Determination**

## Medium

HERO ID: 5441108 Table: 4 of 11

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health

1,1-Dichloroethane

Reproductive/Developmental

**Outcome(s):** 

**Reported Health** 

Histology

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Metric  1: Test Substance Identity 2: Test Substance Source 3: Test Substance Purity  4: Negative and Vehicle Controls 5: Positive Controls 6: Randomized Allocation of Animatication	Rating High Low Medium High N/A mals Low	Comments  The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)  The test substance source was not reported and the identity was not analytically verified by the performing laboratory  Reported as technical grade; no additional information provided.  Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.  A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.  Allocation of test animals was not reported.
22: Test Substance Source 23: Test Substance Purity 24: Negative and Vehicle Controls 25: Positive Controls 26: Randomized Allocation of Animation	Low Medium High N/A	ture, and CASRN)  The test substance source was not reported and the identity was not analytically verified by the performing laboratory  Reported as technical grade; no additional information provided.  Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.  A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
22: Test Substance Source 23: Test Substance Purity 24: Negative and Vehicle Controls 25: Positive Controls 26: Randomized Allocation of Animation	Low Medium High N/A	ture, and CASRN)  The test substance source was not reported and the identity was not analytically verified by the performing laboratory  Reported as technical grade; no additional information provided.  Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.  A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
23: Test Substance Purity 24: Negative and Vehicle Controls 25: Positive Controls 26: Randomized Allocation of Animation	Medium High N/A	by the performing laboratory Reported as technical grade; no additional information provided.  Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.  A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
24: Negative and Vehicle Controls 25: Positive Controls 26: Randomized Allocation of Animation	High N/A	Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.  A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
2 5: Positive Controls 2 6: Randomized Allocation of Animation	N/A	controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.  A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
2 5: Positive Controls 2 6: Randomized Allocation of Animation	N/A	controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.  A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
6: Randomized Allocation of Animation		A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
cation	mals Low	Allocation of test animals was not reported.
Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
e 8: Consistency of Exposure	Low	Gavage volumes not reported
Administration Reporting of Doses/Concentration	ions Medium	Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
Exposure Frequency and Durate	ion High	Dosing administration/frequency was generally 5 days/week, Animals were treated 5 days/week for 78 weeks
	ips and Medium	Doses and spacing were determined based on preliminary studies. However, no reasoning was provided for the change in doses throughout the study.
2 12: Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance
: 13: Test Animal Characteristics	High	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.
	8: Consistency of Exposure Administration 9: Reporting of Doses/Concentrat  10: Exposure Frequency and Durat  11: Number of Exposure Groupose/Concentration Spacing 12: Exposure Route and Method	8: Consistency of Exposure Low Administration 9: Reporting of Doses/Concentrations Medium  10: Exposure Frequency and Duration High 11: Number of Exposure Groups and Dose/Concentration Spacing 12: Exposure Route and Method High

## Human Health Hazard Animal Toxicology Evaluation

#### ... continued from previous page

Study Citation: Health NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Reproductive/Developmental

**Outcome(s):** 

Reported Health

Histology

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks; Mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 544110

HERO ID:	5441108			
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	50/sex in the treatment groups (20/sex controls)
Domain 5: Outcom	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The endpoint was consistently assessed across all groups.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate. In some cases, the number of animals/group evaluated differed due to exclusion of animals that died early, or missing or cannibalized, or partially autolyzed animals
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study result
	Metric 20:	Negative Control Response	Low	In females, the incidence incidences of ovarian cysts and cystic hyperplasia in the uterus were very high (e.g. $> 30\%$ ) in the untreated and vehicle control groups, making it difficult to detect an effect of treatment. Control responses in males were adequate.
Domain 6: Confour	nding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Sufficient data were provided to conduct an independent statistical analysis.
	Metric 24:	Reporting of Data	High	Histology incidence data for this organ/system were adequately reported.

# **Overall Quality Determination**

# High

HERO ID: 5441108 Table: 5 of 11

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Mortality; Renal/Kidney;

**Outcome(s):** 

**Reported Health** 

Mortality: Survival; Renal/Kidney: Histology;

**Effect(s):** 

Health

**Duration:** Chronic (>91 days) 78 weeks; Mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)
	Metric 2:	Test Substance Source	Low	All Outcomes: The test substance source was not reported and the identity was not analytically verified by the performing laboratory
	Metric 3:	Test Substance Purity	Medium	All Outcomes: Reported as technical grade; no additional information provided.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Allocation of test animals was not reported.
Domain 3: Exposure Ch	naracterization Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Gavage volumes not reported
	Metric 9:	Reporting of Doses/Concentrations	Medium	Mortality: Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was provided. Doses were not analytically verified.; Renal/Kidney: Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Animals were treated 5 days/week for 78 weeks
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Doses and spacing were determined based on preliminary studies. However, no reasoning was provided for the change in doses throughout the study.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance

Domain 4: Test Animals

		contin	ued from p	revious page
Study Citation: Health Outcome(s):	NTP (1978). Mortality; Ro		e carcinogei	nicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103
Reported Health Effect(s):	Mortality: Su	urvival; Renal/Kidney: Histology;		
Duration: Chemical: HERO ID:	•	d days) 78 weeks; Mice sethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 50/sex in the treatment groups (20/sex controls)
Domain 5: Outcome A	Assessment Metric 16:	Outcome Assessment Methodology	High	Mortality: Survival was recorded for all animals; Renal/Kidney: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Mortality: The endpoint was consistently assessed across all groups; Renal/Kidney: The endpoint was consistently assessed across all groups.
	Metric 18:	Sampling Adequacy	High	Mortality: Reported information indicates the study used adequate sampling for the outcome(s) of interest; Renal/Kidney: Sampling was adequate. In some cases, the number of animals/group evaluated differed due to exclusion of animals that died early, or missing or cannibalized, or partially autolyzed animals
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this study result
	Metric 20:	Negative Control Response	Medium	Mortality: The biological responses of the negative vehicle control group appeared to be adequate. Survival of untreated control male mice was reported to be low (55% survived less than 74 weeks). No further discussion was provided.; Renal/Kidney: In males, there were differences in response between untreated and solvent controls) that are unlikely to have a substantial impact on results. Responses in females were adequate.
Domain 6: Confoundi	ng / Varjable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Mortality: Detailed statistical methods were reported and were appropriate for the datasets.; Renal/Kidney: Sufficient data were provided to conduct an independent statistical analysis.
		Health Outcomes Unrelated to Exposure  Data Presentation and Analysis		ences) among study groups in the above listed confounding factors.  All Outcomes: There was no information either to support or dismiss the suggithere were differences among groups in animal attrition or health outcomes un exposure (e.g., infection) that could influence the outcome assessment.  Mortality: Detailed statistical methods were reported and were appropriate for datasets.; Renal/Kidney: Sufficient data were provided to conduct an independ tistical analysis.

1,1-Dichloroethane

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**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

HERO ID: 5441108 Table: 5 of 11

Health

Mortality; Renal/Kidney;

**Outcome(s):** 

**Reported Health** Mortality: Survival; Renal/Kidney: Histology;

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Mice

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	High	Mortality: Survival data were reported graphically as "probability of survival", and additional results were described in the text. Statistical results were not reported in association with the probability graphs but results were reported in the text.; Renal/Kidney: Histology incidence data for this organ/system were adequately reported.

# Overall Quality Determination High

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 5441108 Table: 6 of 11

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health Neurological/Behavioral

**Outcome(s):** 

**Reported Health** 

Behavior, signs of toxic effects, histopathological analysis of the nervous system

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Mice

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Comments
e., chemical of interest) was identified definitively (i.e., nomencla
urce was not reported and the identity was not analytically verified poratory
grade; no additional information provided.
1) and untreated control groups were included. *Note, the untreate the same median birth date as the other groups and were added to s after the initial start date.
not explicitly required by the NTP cancer bioassay guideline, but ler certain circumstances.
mals was not reported.
ration and storage was not reported and lack of details could sub- ilts (e.g. storage for long-term studies, preparation for volatile or cals).
reported
ated and changed throughout the study (e.g., rats were dosed with y for the first 7 weeks, then doses were increased to 150 and 75 at 10 weeks, and then reduced again for the remainder of the ation was described for mice. All dosing, however, was clearly was also provided. Doses were not analytically verified.
5 days/week for 78 weeks
ere determined based on preliminary studies. However, no reason- the change in doses throughout the study.
d of exposure were reported and were suited to the test substance
election of the animal species/strain was provided, and the animal this study. Species, strain, ages, sex, and sources were reported. s were not reported, but could be determined from the growth ovided.

		continu	ıed from previ	ous page				
Study Citation: Health		NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103. Neurological/Behavioral						
Outcome(s): Reported Health Effect(s):	Behavior, sig	gns of toxic effects, histopathological analysis	s of the nervou	s system				
Duration: Chemical: HERO ID:	Chronic (>91 days) 78 weeks; Mice 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 5441108							
Domain		Metric	Rating	Comments				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.				
	Metric 15:	Number of Animals per Group	Medium	50/sex in the treatment groups (20/sex controls)				
Domain 5: Outcome	∆ ssessment							
Bonnain 3. Gutcome 2	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology generally addressed the intended outcome(s) of interest. However, the text indicates animals were only observed for behavioral and clinical signs of toxicity weekly for the first 10 weeks, and monthly thereafter. Guidelines indicate that animals should be observed daily. Histopathology of related organs/tissues was appropriate.				
	Metric 17: Metric 18:	Consistency of Outcome Assessment Sampling Adequacy	High Medium	The endpoint was consistently assessed across all groups  It is unclear if sampling was adequate for behavioral/clinical signs because detailed results were not provided. Sampling for histology was appropriate				
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study result				
	Metric 20:	Negative Control Response	Medium	Sores on the body or extremities and generalized and/or localized alopecia was observed in all male groups (including controls) and persisted throughout the study.				
Domain 6: Confound	ing / Variable Co	ntrol						
zomani or comound	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.				
	Metric 23:	Data Presentation and Analysis	Low	Statistical analyses of observational data were not performed (or not described in the methods). Non-neoplastic lesion incidence data are provided for independent review				
	Metric 24:	Reporting of Data	Low	Results of behavioral/clinical signs were loosely described in the text (no incidence or severity data were provided, no mention of statistical significance, and results were not specified for each study group). Non-neoplastic histology data were adequately reported.				

# **Overall Quality Determination**

# Medium

HERO ID: 5441108 Table: 7 of 11

Study Citation: NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health Cardiovascular; Cancer/Carcinogenesis; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Skin/Connective Tissue; Endocrine (Endocrine);

**Outcome(s):** 

Effect(s):

Reported Health

Cardiovascular: Histology; Cancer/Carcinogenesis: Tumor formation; Gastrointestinal: Histology; Immune/Hematological: Histology; Hepatic/Liver:

Histology; Skin/Connective Tissue: Histology; Endocrine (Endocrine): Adrenal, pituitary histology;

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)
	Metric 2:	Test Substance Source	Low	All Outcomes: The test substance source was not reported and the identity was not analytically verified by the performing laboratory
	Metric 3:	Test Substance Purity	Medium	All Outcomes: Reported as technical grade; no additional information provided.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Both vehicle (corn oil) and untreated control groups were included.  *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Allocation of test animals was not reported.
Domain 3: Exposure Ch				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure	Low	All Outcomes: Gavage volumes were not reported.
		Administration	3.6.11	
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: Dosing administration/frequency was generally 5 days/week, however, starting on week 36, intubation ceased for all treated animals for 1 week, followed by 4 weeks of dose administration. This pattern continued for the remainder of the dosing period. Justification for these changes was not provided, and this pattern of dosing is atypical for a chronic study. All animals that survived, were dosed through 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Doses and spacing were determined based on a preliminary study but were changed up to three times throughout the study without justification.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance

Domain 4: Test Animals

HERO ID: 5441108 Table: 7 of 11

#### ... continued from previous page

Study Citation:
NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health Cardiovascular; Cancer/Carcinogenesis; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Skin/Connective Tissue; Endocrine (Endocrine);
Outcome(s):

Reported Health Cardiovascular: Histology; Cancer/Carcinogenesis: Tumor formation; Gastrointestinal: Histology; Immune/Hematological: Histology; Hepatic/Liver: Histology; Skin/Connective Tissue: Histology; Endocrine (Endocrine): Adrenal, pituitary histology;

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

HERO ID:	5441108			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 50/sex in the treatment groups (20/sex controls)
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The endpoint was consistently assessed across all groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate. In some cases, the number of animals/group evaluated differed due to exclusion of animals that died early, or missing or cannibalized, or partially autolyzed animals
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this study result
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).
Domain 6: Confound	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	All Outcomes: Rats from all study groups (including both sexes and controls) exhibited high incidences of pneumonia (up to 95%), indicating infections in these animals. This was not discussed or mentioned by the study authors. It is unclear how these infections impacted study results.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Sufficient data were provided to conduct an independent statistical analysis.
	Metric 24:	Reporting of Data	High	All Outcomes: Histology incidence data for this organ/system were adequately reported.

## **Overall Quality Determination**

## Uninformative

Health

HERO ID: 5441108 Table: 8 of 11

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Mortality; Thyroid;

**Outcome(s):** 

Reported Health

Mortality: Survival; Thyroid: Histology;

**Effect(s):** 

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)
	Metric 2:	Test Substance Source	Low	All Outcomes: The test substance source was not reported and the identity was not analytically verified by the performing laboratory
	Metric 3:	Test Substance Purity	Medium	All Outcomes: Reported as technical grade; no additional information provided.
Domain 2: Test Design				
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Allocation of test animals was not reported.
Domain 3: Exposure C				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure Administration	Low	Mortality: Dose volumes were not reported.; Thyroid: Gavage volumes were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: Dosing administration/frequency was generally 5 days/week, however, starting on week 36, intubation ceased for all treated animals for 1 week, followed by 4 weeks of dose administration. This pattern continued for the remainder of the dosing period. Justification for these changes was not provided, and this pattern of dosing is atypical for a chronic study. All animals that survived, were dosed through 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Doses and spacing were determined based on a preliminary study but were changed up to three times throughout the study without justification.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance

Domain 4: Test Animals

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103. **Study Citation:** Mortality; Thyroid;

Health

**Outcome(s):** 

Reported Health

Mortality: Survival; Thyroid: Histology;

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	5441108			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 50/sex in the treatment groups (20/sex controls)
Domain 5: Outcome A	ssessment			
Domain 3. Sulcome 1.	Metric 16:	Outcome Assessment Methodology	High	Mortality: Survival was recorded for all animals; Thyroid: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Mortality: The endpoint was consistently assessed across all groups; Thyroid: The endpoint was consistently assessed across all groups.
	Metric 18:	Sampling Adequacy	High	Mortality: Reported information indicates the study used adequate sampling for the outcome(s) of interest; Thyroid: Sampling was adequate. In some cases, the number of animals/group evaluated differed due to exclusion of animals that died early, or missing or cannibalized, or partially autolyzed animals
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this study result
	Metric 20:	Negative Control Response	Medium	Mortality: It was noted that vehicle controls for male rats had greater mortality than the low dose males during the early portion of the study. Untreated control male mice also showed low survival (55% survived less than 74 weeks). No possible explanations were provided beyond a statement indicating that: "During the last 26 weeks of the study, the decreased survival for the controls was probably due to chronic respiratory and renal involvement." Control mortality did not appear to impact the ability to observe increases in tumor incidence.; Thyroid: There were significant differences in response between the untreated and vehicle control groups for this outcome of interest.
Domain 6: Confoundir	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	All Outcomes: Rats from all study groups (including both sexes and controls) exhibited high incidences of pneumonia (up to 95%), indicating infections in these animals. This was not discussed or mentioned by the study authors. It is unclear how these infections impacted study results.
		Con	ntinued on next page .	

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

HERO ID: 5441108 Table: 8 of 11

**Health** Mortality; Thyroid;

**Outcome(s):** 

Reported Health Mortalit

Mortality: Survival; Thyroid: Histology;

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	High	Mortality: Detailed statistical methods were reported and were appropriate for the datasets.; Thyroid: Sufficient data were provided to conduct an independent statistical analysis.
	Metric 24:	Reporting of Data	High	Mortality: Survival data were reported graphically as "probability of survival", and additional results were described in the text. Statistical results were not reported in association with the probability graphs but results were reported in the text.; Thyroid: Histology incidence data for this organ/system were adequately reported.

## **Overall Quality Determination**

## Uninformative

HERO ID: 5441108 Table: 9 of 11

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health

Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Bodyweight, food consumption

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and the identity was not analytically verified by the performing laboratory
-	Metric 3:	Test Substance Purity	Medium	Reported as technical grade; no additional information provided.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	Allocation of test animals was not reported.
Domain 3: Exposure C	haracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could sub- stantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure	Low	Gavage volumes were not reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	Low	Dosing administration/frequency was generally 5 days/week, however, starting on week 36, intubation ceased for all treated animals for 1 week, followed by 4 weeks of dose administration. This pattern continued for the remainder of the dosing period. Justification for these changes was not provided, and this pattern of dosing is atypical for a chronic study. All animals that survived, were dosed through 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Doses and spacing were determined based on a preliminary study but were changed up to three times throughout the study without justification.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance

Domain 4: Test Animals

**Study Citation:** NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103. Nutritional/Metabolic

Health

**Outcome(s):** Reported Health

Bodyweight, food consumption

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID: 5441108

HERO ID:	5441108			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	50/sex in the treatment groups (20/sex controls)
Domain 5: Outcome	e Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The endpoint was consistently assessed across all groups
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study result
	Metric 20:	Negative Control Response	Medium	Some differences in the untreated and vehicle control groups were observed
Domain 6: Confoun	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	Rats from all study groups (including both sexes and controls) exhibited high incidences of pneumonia (up to 95%), indicating infections in these animals. This was not discussed or mentioned by the study authors. It is unclear how these infections impacted study results.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analyses of body weight data were not performed. Data could potentially be extracted from growth curves, but the number of animals for each data point is not reported.
	Metric 24:	Reporting of Data	Low	Bodyweight data were reported graphically as growth curves in the absence of measures of variance. No statistical results were reported, and the text indicates that Fluctuations in the growth curves may be due to mortality; as the size of the group diminishes, the mean body weight may be subject to wide variations. Food consumption was supposedly monitored but results were not reported.

1,1-Dichloroethane Human Health Hazard Animal Toxicology Evaluation HERO ID: 5441108 Table: 9 of 11

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Study Citation: NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health Nutritional/Metabolic

**Outcome(s):** 

Reported Health Bodyweight, food consumption

Effect(s): Duration:

Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain Metric Rating Comments

Overall Quality Determination Uninformative

Study Citation: Health NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

HERO ID: 5441108 Table: 10 of 11

Renal/Kidney; Reproductive/Developmental; Lung/Respiratory;

**Outcome(s):** 

Reported Health

Renal/Kidney: Histology; Reproductive/Developmental: Histology; Lung/Respiratory: Histology;

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)
	Metric 2:	Test Substance Source	Low	All Outcomes: The test substance source was not reported and the identity was not analytically verified by the performing laboratory
	Metric 3:	Test Substance Purity	Medium	All Outcomes: Reported as technical grade; no additional information provided.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Allocation of test animals was not reported.
Domain 2. Evmasuma C	Thomostoniantion			
Domain 3: Exposure C	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage was not reported and lack of details could substantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Gavage volumes were not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: Dosing administration/frequency was generally 5 days/week, however, starting on week 36, intubation ceased for all treated animals for 1 week, followed by 4 weeks of dose administration. This pattern continued for the remainder of the dosing period. Justification for these changes was not provided, and this pattern of dosing is atypical for a chronic study. All animals that survived, were dosed through 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Doses and spacing were determined based on a preliminary study but were changed up to three times throughout the study without justification.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance

Domain 4: Test Animals

Study Citation: Health NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

HERO ID: 5441108 Table: 10 of 11

Renal/Kidney; Reproductive/Developmental; Lung/Respiratory;

**Outcome(s):** 

Reported Health

Renal/Kidney: Histology; Reproductive/Developmental: Histology; Lung/Respiratory: Histology;

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

HERO ID:	5441108			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 50/sex in the treatment groups (20/sex controls)
Domain 5: Outcome	Assessment			
Bonain 3. Guccome	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The endpoint was consistently assessed across all groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate. In some cases, the number of animals/group evaluated differed due to exclusion of animals that died early, or missing or cannibalized, or partially autolyzed animals
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this study result
	Metric 20:	Negative Control Response	Uninformative	Renal/Kidney: Untreated and vehicle controls had high incidences ( $>30\%$ ) of kidney lesions making it difficult to detect and effect of treatment.; Reproductive/Developmental: The incidence of the outcome of interest was very high (e.g. $>30\%$ ) in the control groups, making it difficult to detect an effect of treatment.; Lung/Respiratory: The incidence of the outcome of interest is very high (e.g. $>30\%$ ) in the control group, making it difficult to detect an effect of treatment.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	All Outcomes: Rats from all study groups (including both sexes and controls) exhibited high incidences of pneumonia (up to 95%), indicating infections in these animals. This was not discussed or mentioned by the study authors. It is unclear how these infections impacted study results.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Sufficient data were provided to conduct an independent statistical analysis.
	Metric 24:	Reporting of Data	High	All Outcomes: Histology incidence data for this organ/system were adequately reported.

Human Health Hazard Animal Toxicology Evaluation 1,1-Dichloroethane

HERO ID: 5441108 Table: 10 of 11

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NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103. **Study Citation:** 

Health Renal/Kidney; Reproductive/Developmental; Lung/Respiratory;

**Outcome(s):** 

**Reported Health** Renal/Kidney: Histology; Reproductive/Developmental: Histology; Lung/Respiratory: Histology;

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain Metric Rating Comments

**Overall Quality Determination** Uninformative Health

HERO ID: 5441108 Table: 11 of 11

**Study Citation:** 

NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Neurological/Behavioral

**Outcome(s):** 

Reported Health

Behavior, signs of toxic effects, histopathological analysis of the nervous system

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	The test substance (i.e., chemical of interest) was identified definitively (i.e., nomenclature, and CASRN)
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and the identity was not analytically verified by the performing laboratory
	Metric 3:	Test Substance Purity	Medium	Reported as technical grade; no additional information provided.
Domain 2: Test Desig	αn			
Domain 2. Test Desig	Metric 4:	Negative and Vehicle Controls	High	Both vehicle (corn oil) and untreated control groups were included. *Note, the untreated controls did not have the same median birth date as the other groups and were added to the study a few weeks after the initial start date.
	Metric 5:	Positive Controls	N/A	A positive control is not explicitly required by the NTP cancer bioassay guideline, but may be desirable under certain circumstances.
	Metric 6:	Randomized Allocation of Animals	Low	Allocation of test animals was not reported.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage was not reported and lack of details could sub- stantially impact results (e.g. storage for long-term studies, preparation for volatile or low-solubility chemicals).
	Metric 8:	Consistency of Exposure	Low	Gavage volumes were not reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	Medium	Dosing was complicated and changed throughout the study (e.g., rats were dosed with 100 and 50 mg/kg/day for the first 7 weeks, then doses were increased to 150 and 75 mg/kg/day for the next 10 weeks, and then reduced again for the remainder of the study). A similar situation was described for mice. All dosing, however, was clearly reported, and a TWA was also provided. Doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	Low	Dosing administration/frequency was generally 5 days/week, however, starting on week 36, intubation ceased for all treated animals for 1 week, followed by 4 weeks of dose administration. This pattern continued for the remainder of the dosing period. Justification for these changes was not provided, and this pattern of dosing is atypical for a chronic study. All animals that survived, were dosed through 78 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Doses and spacing were determined based on a preliminary study but were changed up to three times throughout the study without justification.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance

Domain 4: Test Animals

**Study Citation:** NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103. Neurological/Behavioral

Health

**Outcome(s):** 

Reported Health

Behavior, signs of toxic effects, histopathological analysis of the nervous system

Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

HERO ID:	3441106			
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	High	Justification for the selection of the animal species/strain was provided, and the animals were appropriate for this study. Species, strain, ages, sex, and sources were reported. Starting body weights were not reported, but could be determined from the growth curves graphically provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Detailed animal husbandry conditions were provided and were adequate. It was noted that treated animals were housed in a room with animals from other studies that were treated with other compounds, but this is not expected to have a significant impact on study results.
	Metric 15:	Number of Animals per Group	Medium	50/sex in the treatment groups (20/sex controls)
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology addressed the intended outcome(s) of interest, however, the text indicates animals were only observed for behavioral and clinical signs of toxicity weekly for the first 10 weeks, and monthly thereafter. Guidelines indicate that animals should be observed daily. Histopathology of related organs/tissues was appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	The endpoint was consistently assessed across all groups
	Metric 18:	Sampling Adequacy	Medium	It is unclear if sampling was adequate for behavioral/clinical signs because detailed results were not provided.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study result
	Metric 20:	Negative Control Response	Low	Biological responses for the negative control group were not reported for behavioral/clincial signs
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences (or identified only minor differences) among study groups in the above listed confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	Rats from all study groups (including both sexes and controls) exhibited high incidence of pneumonia (up to 95%), indicating infections in these animals. This was not discussed or mentioned by the study authors. It is unclear how these infections impacted study results.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analyses of observational data were not performed. non-Neoplastic lesion incidence data are provided for independent review, however, data were not provided for clinical observations precluding the ability to independently assess this data
	Metric 24:	Reporting of Data	Medium	Results of behavioral/clinical signs were loosely described in the text (no incidence or severity data were provided). Non-neoplastic histology data were adequately reported.

HERO ID: 5441108 Table: 11 of 11

Human Health Hazard Animal Toxicology Evaluation

1,1-Dichloroethane

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Study Citation: NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.

Health Neurological/Behavioral

Outcome(s):

Behavior, signs of toxic effects, histopathological analysis of the nervous system

Reported Health Effect(s):

**Duration:** Chronic (>91 days) 78 weeks; Rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5441108

Domain Metric Rating Comments

Overall Quality Determination Uninformative

HERO ID: 62617 Table: 1 of 18

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Mortality (This form is for rats)

**Outcome(s):** 

**Reported Health** Death

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

	Metric	Rating	Comments
ce			
Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
Metric 5:	Positive Controls	N/A	Not necessary for the study type
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
	D	T	
Metric 7:	Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)
	Metric 1: Metric 2: Metric 3:  Metric 4: Metric 5: Metric 6:  aracterization Metric 7:  Metric 8:	Metric 1: Test Substance Identity  Metric 2: Test Substance Source  Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls  Metric 5: Positive Controls  Metric 6: Randomized Allocation of Animals  aracterization  Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations  Metric 10: Exposure Frequency and Duration	Metric 1: Test Substance Identity High  Metric 2: Test Substance Source High  Metric 3: Test Substance Purity High  Metric 4: Negative and Vehicle Controls High  Metric 5: Positive Controls N/A  Metric 6: Randomized Allocation of Animals Low  aracterization  Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations High

## ... continued from previous page

**Study Citation:** 

Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Mortality (This form is for rats)

**Outcome(s):** 

Reported Health

Death

Effect(s):

**Duration:** 

Chronic (>91 days) Chronic; rats

Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

02017			
	Metric	Rating	Comments
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.
Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
als			
Metric 13:	Test Animal Characteristics	Low	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
Metric 15:	Number of Animals per Group	Low	For exposure groups, animal numbers consisted of 15 rats/sex/group; 20/sex/group is considered appropriate for a chronic study.
Assessment			
Metric 16:	Outcome Assessment Methodology	High	Details of methods relevant to this organ/system were adequately described.
Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
Metric 18:	Sampling Adequacy	High	Specific details regarding sampling of outcomes were clearly reported for some, but not all endpoints. For example, the text indicates that "in many cases" blood was collected at the time of autopsy, and "in many cases" a portion of the liver was frozen for lipid analysis. It is unclear if this means samples were only collected from some animals? From the mid-exposure level data the number of rats used for body weight and organ weights was less than the number of animals exposed, however, no mortalities in these groups were reported. For histopathology, the text indicates that "all survivors were examined for evidence of organic injury." For this endpoint, however, all animals were observed for mortality.
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
Metric 20:	Negative Control Response	Low	Mortality data from control groups were not reported.
ng / Variable Co	ntrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.
	Continu	ied on next pa	age
	Metric 11:  Metric 12:  Als  Metric 13:  Metric 14:  Metric 15:  Assessment  Metric 16:  Metric 17:  Metric 18:  Metric 19:  Metric 20:  ang / Variable Con	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Als  Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group  Assessment  Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  mg / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method Low  Metric 13: Test Animal Characteristics Low  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group Low  Assessment  Metric 16: Outcome Assessment Methodology High Metric 17: Consistency of Outcome Assessment Low  Metric 18: Sampling Adequacy High  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response Low  Metric 21: Confounding Variables in Test Design Medium

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Mortality (This form is for rats)

Outcome(s):

Reported Health

Death

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
	Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant.
	Metric 24:	Reporting of Data	Low	For the mid and low exposure groups, Data for this endpoint were only described in the text indicating "no adverse effects observed." For a chronic duration study, it is expected that some animals in both the experimental and control groups would die. The number of deaths per group was not reported.

## **Overall Quality Determination**

HERO ID: 62617 Table: 2 of 18

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Hepatic/Liver (This form is for rats)

Outcome(s):

Reported Health

Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol

**Effect(s):** 

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig	an.			
Domain 2: Test Desig	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure	Characterization			
Zoman et Zaposare	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)

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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Hepatic/Liver (This form is for rats)

**Outcome(s):** 

**Reported Health** Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

HERO ID:	62617			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Low	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
	Metric 15:	Number of Animals per Group	Low	For exposure groups, animal numbers consisted of 15 rats/sex/group; 20/sex/group is considered appropriate for a chronic study.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Details of methods relevant to this organ/system were adequately described.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
	Metric 18:	Sampling Adequacy	Low	Specific details regarding sampling of outcomes were clearly reported for some, but not all endpoints. For example, the text indicates that "in many cases" blood was collected at the time of autopsy, and "in many cases" a portion of the liver was frozen for lipid analysis. It is unclear if this means samples were only collected from some animals? From the mid-exposure level data the number of rats used for body weight and organ weights was less than the number of animals exposed, however, no mortalities in these groups were reported. For histopathology, the text indicates that "all survivors were examined for evidence of organic injury."
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Low	Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g., hematology, histology) because no data were provided. There was no indication in the text that results from control groups were unexpected.
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.

and Procedures

HERO ID: 62617 Table: 2 of 18

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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Hepatic/Liver (This form is for rats)

Outcome(s):

Reported Health

Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol

Effect(s):
Duration:

Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
	Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant.
	Metric 24:	Reporting of Data	Low	Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability for the mid exposure level only. In some cases, (e.g., serum parameters) it is not clearly reported which control group was used for comparisons (i.e, descriptions only indicate "controls").

## **Overall Quality Determination**

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Lung/Respiratory (This form is for Guinea pigs)

**Outcome(s):** 

Reported Health

Gross examinations; histology; organ weights

**Effect(s):** 

**Duration:**Chronic (>91 days) Chronic; Guinea pigs**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig	on			
Johnan 2. Test Desig	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g. test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)

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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Lung/Respiratory (This form is for Guinea pigs)

**Outcome(s):** 

Reported Health

Gross examinations; histology; organ weights

Effect(s): Duration:

Duration:Chronic (>91 days) Chronic; Guinea pigsChemical:1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

HERO ID.	02017			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	Low	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
	Metric 15:	Number of Animals per Group	Low	For exposure groups, animal numbers consisted of 8/sex/group; This is lower than the recommended 20/sex/group considered appropriate for a chronic study in rodents.
Domain 5: Outcome As	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	Details of methods relevant to this organ/system were adequately described.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
	Metric 18:	Sampling Adequacy	Medium	For organ weights, the methods do not specifically indicate how many animals were assessed per group. From the data tables shown, the number of animals varied between 5-8 which was sufficient for statistical analysis.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Medium	Details of the biological responses of controls appeared to be appropriate for the data provided (organ weights).
Domain 6: Confoundin	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
	Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant.

HERO ID: 62617 Table: 3 of 18

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**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Lung/Respiratory (This form is for Guinea pigs) Health

**Outcome(s): Reported Health** 

Gross examinations; histology; organ weights

Effect(s):

Chronic (>91 days) Chronic; Guinea pigs **Duration:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Low	Quantal data was provided for body weights and relative organ weights only (reported as
				means in the absence of measures of variability)

#### **Overall Quality Determination** Medium

HERO ID: 62617 Table: 4 of 18

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Lung/Respiratory (This form is for rats)

**Outcome(s):** 

**Reported Health** Gross examinations; histology; organ weights

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig	n			
Domain 2. Test Desig	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure (	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Lung/Respiratory (This form is for rats)

Outcome(s):

Reported Health

Gross examinations; histology; organ weights

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

	6261/			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Animal	ls			
	Metric 13:	Test Animal Characteristics	Low	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
	Metric 15:	Number of Animals per Group	Low	For exposure groups, animal numbers consisted of 15 rats/sex/group; 20/sex/group is considered appropriate for a chronic study.
Domain 5: Outcome A	ssessment			
Domain 3. Gateome 71	Metric 16:	Outcome Assessment Methodology	High	Details of methods relevant to this organ/system were adequately described.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the un certainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
	Metric 18:	Sampling Adequacy	Medium	For organ weights, the methods do not specifically indicate how many animals were assessed per group. From the data table shown for the mid-exposure level, at least 9 exposed and 11 control animal organ weights were measured, which is sufficient for the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Medium	Details of the biological responses of controls appeared to be appropriate for the data provided (organ weights).
Domain 6: Confoundin	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Lung/Respiratory (This form is for rats)

Outcome(s):

**Reported Health** Gross examinations; histology; organ weights

**Effect(s):** 

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Low	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant; however, no statistical analysis was included in the report for the data provided.
	Metric 24:	Reporting of Data	Low	Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability); only data for the mid exposure was provided. At the lowest exposure level, the study states no adverse effects observed.

## Overall Quality Determination Medium

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Immune/Hematological (This form is for Guinea pigs)

Outcome(s): Reported Health

Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.

Effect(s):

**Duration:**Chronic (>91 days) Chronic; Guinea pigs**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desi	an			
Domain 2. Test Desi	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure	Characterization			
Domain or Enposure	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected. At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 170 days and females went 226 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
Health	Immune/Hematological (This form is for Guinea pigs)

Outcome(s): Reported Health

Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.

Effect(s):

**Duration:**Chronic (>91 days) Chronic; Guinea pigs**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	62617			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying; this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Low	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
	Metric 15:	Number of Animals per Group	Low	For exposure groups, animal numbers consisted of 8/sex/group; this is lower than the 20/sex/group considered appropriate for a chronic study.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Methods for endpoint-related serum chemistry or hematology were not clearly reported. The methods indicate "in many cases" blood was collected at the time of autopsy. Therefore, the numbers and groups in which samples were collected are not clear.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
	Metric 18:	Sampling Adequacy	Low	For organ weights, the number of animals assessed per group varied, (5-8 animals), but was sufficient for statistical analysis. The adequacy of sampling for serum chemistry and hematology endpoints is unclear. The methods only indicate that blood samples were taken "in many cases"
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Low	Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g, hematology, histology) because no data were provided. There was no indication in the text that results from control groups were unexpected. Control organ weight results appear to be appropriate.
Domain 6: Confoundin	og / Variable Co	ntral		
Domain 6: Confounding	Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.
	WIGUIC 21.	and Procedures	Mediuili	No confounding variables were reported.
		Continu	ued on next pa	age

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
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Health
Outcome(s):

Immune/Hematological (This form is for Guinea pigs)

Reported Health

Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.

**Effect(s):** 

**Duration:**Chronic (>91 days) Chronic; Guinea pigs**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
	Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant.
	Metric 24:	Reporting of Data	Low	Quantal data was provided for relative organ weights only (reported as means in the absence of measures of variability for the mid exposure level only. Results for measurement of prothrombin clotting time and hematological measurements, and related histopathology were described as non-adverse in the text.

# **Overall Quality Determination**

HERO ID: 62617 Table: 6 of 18

1,1-Dichloroethane

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Nutritional/Metabolic (This form is for Guinea pigs)

Outcome(s):

Reported Health

Body weight; food consumption

Effect(s):

**Duration:**Chronic (>91 days) Chronic; Guinea pigs**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design	n			
	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separat concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
D : 2 E (	71			
Domain 3: Exposure C		D (1 10) CT (	т	
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥170 days. At the high exposure level, all of the animals died, so at this level, the overall duration was shorter than expected (32 days for females and 14 days for males). At the mid-exposure level, animals "tolerated" exposure for 246 days, and at the low exposure level, males went 170 days and females went 226 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Nutritional/Metabolic (This form is for Guinea pigs)

**Outcome(s):** 

Reported Health

Body weight; food consumption

Effect(s):

**Duration:**Chronic (>91 days) Chronic; Guinea pigs**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

- ·	62617			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	Low	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
	Metric 15:	Number of Animals per Group	Low	For exposure groups, animal numbers consisted of 8/sex/group; Guidelines indicate 20/sex/group is considered appropriate for a chronic study.
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Details of methods relevant to this organ/system were mostly adequately described. Body weights were measured twice weekly, however, it was only reported that "records' were kept for food consumption (no further details provided). The study did not indicate that water consumption was monitored.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
	Metric 18:	Sampling Adequacy	Medium	The study indicated that body weights from EACH animal were collected twice weekly. Details on sampling for food consumption were limited.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Low	Air-only control data for body weights, growth and organ weight endpoints for Males in the low exposure group was not reported; no explanation was provided in the text.
Domain 6: Confounding	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.

HERO ID: 62617 Table: 6 of 18

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**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Nutritional/Metabolic (This form is for Guinea pigs)

**Outcome(s):** 

**Reported Health** Body weight; food consumption

Effect(s):

Chronic (>91 days) Chronic; Guinea pigs **Duration:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant. Results from statistical analysis were shown for body weight and organ weight outcomes.
	Metric 24:	Reporting of Data	Low	Growth charts were included in the absence of statistical analysis. Final body weights were reported as means without measures of variance, and significance was reported. Although food consumption was monitored, the results of this endpoint were not reported.

# **Overall Quality Determination**

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Renal/Kidney (This form is for Guinea pig); Renal/Kidney (This form is for rats);

**Outcome(s):** 

**Reported Health** Renal/Kidney (This form is for Guinea pig): Gross examinations; histology; organ weights; Renal/Kidney (This form is for rats): Gross examinations;

**Effect(s):** histology; organ weights;

**Duration:** Chronic (>91 days) Chronic; Guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure Ch	naracterization			
Domain 3. Exposure Cr	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration

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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Renal/Kidney (This form is for Guinea pig); Renal/Kidney (This form is for rats);

**Outcome(s):** 

**Reported Health** Renal/Kidney (This form is for Guinea pig): Gross examinations; histology; organ weights; Renal/Kidney (This form is for rats): Gross examinations;

**Effect(s):** histology; organ weights;

**Duration:** Chronic (>91 days) Chronic; Guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	62617			
Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	Low	Renal/Kidney (This form is for Guinea pig): Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥170 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (32 days for females and 14 days for males). At the mid-exposure level, animals "tolerated" exposure for 246 days, and at the low exposure level, males went 170 days and females went 248 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups); Renal/Kidney (This form is for rats): Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Renal/Kidney (This form is for Guinea pig): Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying; this exposure level could therefore note be used to evaluate chronic effects.; Renal/Kidney (This form is for rats): Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Animals				
2 Small Test / minitals	Metric 13:	Test Animal Characteristics	Low	Renal/Kidney (This form is for Guinea pig): Animals were obtained from a commercial source, but the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.; Renal/Kidney (This form is for rats): The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to reporting animal diets. No other data were provided.
		Continu	ied on next p	age

		continu	ued from previ	ious page			
Study Citation:  Health Outcome(s): Reported Health Effect(s):	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493. Renal/Kidney (This form is for Guinea pig); Renal/Kidney (This form is for rats);  Renal/Kidney (This form is for Guinea pig): Gross examinations; histology; organ weights; Renal/Kidney (This form is for rats): Gross examination histology; organ weights;						
Duration: Chemical:		Chronic (>91 days) Chronic; Guinea pigs 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 62617						
Domain		Metric	Rating	Comments			
	Metric 15:	Number of Animals per Group	Low	Renal/Kidney (This form is for Guinea pig): For exposure groups, animal numbers consisted of 8/sex/group; this is lower than the 20/sex/group is considered appropriate for a chronic study.; Renal/Kidney (This form is for rats): For exposure groups, animal numbers consisted of 15 rats/sex/group; 20/sex/group is considered appropriate for a chronic study.			
Domain 5: Outcome	Assessment						
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The methods for clinical chemistry related to this endpoint were poorly described. It is reported that at autopsy blood was collected in "many cases"			
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.			
	Metric 18:	Sampling Adequacy	Medium	All Outcomes: For organ weights, the methods do not specifically indicate how many animals were assessed per group. From the data table shown for the mid-exposure level, at least 9 exposed and 11 control animal organ weights were measured, which is sufficient for the outcome of interest. The number of animals used for serum chemistry is not reported. The text indicates that "all animals" were examined microscopically.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the outcomes assessed.			
	Metric 20:	Negative Control Response	Low	All Outcomes: Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g, hematology, histology) because no data were provided. There was no indication in the text that results from control groups were unexpected.			
Domain 6: Confound	ing / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: No confounding variables were reported.			
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.			
	Metric 23:	Data Presentation and Analysis	Low	Renal/Kidney (This form is for Guinea pig): The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant; however, only statistics for comparisons with unexposed controls were provided.; Renal/Kidney (This form is for rats): The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant; however, it is unclear if statistical analysis was applied for the organ weight data for rats because it is not included in the data table.			

azard Animal Toxicology Evaluation HERO ID: 62617 Table: 7 of 18

#### ... continued from previous page

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Renal/Kidney (This form is for Guinea pig); Renal/Kidney (This form is for rats);

**Outcome(s):** 

**Reported Health** Renal/Kidney (This form is for Guinea pig): Gross examinations; histology; organ weights; Renal/Kidney (This form is for rats): Gross examinations;

**Effect(s):** histology; organ weights;

**Duration:** Chronic (>91 days) Chronic; Guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Low	Renal/Kidney (This form is for Guinea pig): Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability. There was no air-only control data reported for males in the low exposure group. Data for related serum chemistry (e.g., BUN) were not provided. It was reported in the text that no changes were observed compared with controls The control group used for comparison of some endpoints was not specified.; Renal/Kidney (This form is for rats): Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability for the mid exposure level only. Data for related serum chemistry (e.g., BUN) were not provided. It was reported in the text that no changes were observed compared with controls The control group used for comparison was not specified.

## **Overall Quality Determination**

HERO ID: 62617 Table: 8 of 18

1,1-Dichloroethane

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Nutritional/Metabolic (This form is for rats)

**Outcome(s):** 

Reported Health

Body weight; food consumption

Effect(s): Duration:

Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig	an.			
Domain 2: Test Desig	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure	Characterization			
Zoman et Zaposare	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on					
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.					

Health

Nutritional/Metabolic (This form is for rats)

Outcome(s):

Reported Health

Body weight; food consumption

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

	62617			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	Low	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
	Metric 15:	Number of Animals per Group	Low	For exposure groups, animal numbers consisted of 15 rats/sex/group; 20/sex/group is considered appropriate for a chronic study.
Domain 5: Outcome As	sessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Details of methods relevant to this organ/system were mostly adequately described. Body weights were measured twice weekly, however, it was only reported that "records" were kept for food consumption (no further details provided). The study did not indicate that water consumption was monitored
	Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
	Metric 18:	Sampling Adequacy	Medium	The study indicated that body weights from EACH animals were collected twice weekly Details on sampling for food consumption was not clearly stated.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Medium	Negative control responses for the data shown appeared to be appropriate.
Domain 6: Confounding	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.

HERO ID: 62617 Table: 8 of 18

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**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Nutritional/Metabolic (This form is for rats)

**Outcome(s):** 

**Reported Health** Body weight; food consumption

Effect(s):

Chronic (>91 days) Chronic; rats **Duration:** 

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Low	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant, however, no statistical analysis was included on the data provided.
	Metric 24:	Reporting of Data	Low	For the mid and low exposure groups, Data for this endpoint were only described in the text indicating "no adverse effects observed." For the mid-exposure group, growth charts were included in the absence of statistical analysis. Final body weights were reported as means without measures of variance, and significance was reported. Although food consumption was monitored, the results of this endpoint were not reported.

# **Overall Quality Determination**

HERO ID: 62617 Table: 9 of 18

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Cardiovascular (This form is for rats)

Outcome(s):

Reported Health

Gross examinations; histology; organ weights

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subs	stance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity ≥99.7 %; the only impurity identified was trichloroethylene.
Damain 2. Test Desi	~			
Domain 2: Test Desi	-			
	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure	Characterization			
Domain or Emposare	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)

## ... continued from previous page

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health Cardiovascular (This form is for rats)

**Outcome(s):** 

**Reported Health** Gross examinations; histology; organ weights

Effect(s):

Chronic (>91 days) Chronic; rats **Duration:** 

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Me Domain 4: Test Animals Me	etric 11: etric 12: etric 13: etric 14:	Metric  Number of Exposure Groups and Dose/Concentration Spacing  Exposure Route and Method  Test Animal Characteristics	Rating High  Low	Comments  Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.  Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Me Domain 4: Test Animals Me	etric 12: etric 13: etric 14:	Dose/Concentration Spacing  Exposure Route and Method	Low	els was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.  Vapor generation was clearly described; however, the airflow rate and the number of air
Domain 4: Test Animals Me	etric 13:	•		
Me	etric 14:	Test Animal Characteristics	Low	
	etric 14:	Test Animal Characteristics	Low	
Me			LOW	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	15	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
Me	etric 15:	Number of Animals per Group	Medium	For exposure groups, animal numbers consisted of 15 rats/sex/group; 20/sex/group is considered appropriate for a chronic study.
Domain 5: Outcome Assessm	ment			
Me	etric 16:	Outcome Assessment Methodology	High	Details of methods relevant to this organ/system were adequately described.
Me	etric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
Ме	etric 18:	Sampling Adequacy	Medium	For organ weights, the methods do not specifically indicate how many animals were assessed per group. From the data table shown for the mid-exposure level, at least 9 exposed and 11 control animal organ weights were measured, which is sufficient for the outcome of interest.
Me	etric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
Me	etric 20:	Negative Control Response	Low	Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g, hematology, histology) because no data were provided. There was no indication in the text that results from control groups were unexpected.
Domain 6: Confounding / Va	ariable Con	ntrol		
	etric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.
Me	etric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Cardiovascular (This form is for rats)

Outcome(s):

**Reported Health** Gross examinations; histology; organ weights

**Effect(s):** 

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Low	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant; however, the data table provided for the mid-dose group does not clearly indicate whether statistical analysis was done.
	Metric 24:	Reporting of Data	Low	Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability for the mid exposure level only. Incidences of histopathology were not reported. Organ weights were provided for the mid-exposure level only.

# **Overall Quality Determination**

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Cardiovascular (This form is for Guinea pigs)

**Outcome(s):** 

Reported Health

Gross examinations; histology; organ weights

**Effect(s):** 

**Duration:** Chronic (>91 days) Chronic; Guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design				
S	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥170 days. At the high exposure level, all of the animals died, so at this level, the overall duration was shorter than expected (32 days for females and 14 days for males). At the mid-exposure level, animals "tolerated" exposure for 246 days, and at the low exposure level, males went 170 days and females went 226 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)
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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Cardiovascular (This form is for Guinea pigs)

Outcome(s):

Reported Health

Gross examinations; histology; organ weights

Effect(s):
Duration:

**Duration:** Chronic (>91 days) Chronic; Guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

62617			
	Metric	Rating	Comments
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying; this exposure level could, therefore, could not be used to evaluate chronic effects.
Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Metric 13:	Test Animal Characteristics	Low	Animals were obtained from an unspecified commercial source. The animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
Metric 14:	Adequacy and Consistency of Animal	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
Metric 15:	Number of Animals per Group	Medium	For exposure groups, animal numbers consisted of 8/sex/group; this is lower than the recommended 20/sex/group is considered appropriate for a chronic study in rodents.
ssment			
Metric 16:	Outcome Assessment Methodology	High	Details of methods relevant to this organ/system were adequately described.
Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
Metric 18:	Sampling Adequacy	Medium	For organ weights, the methods do not specifically indicate how many animals were assessed per group, but the number of animals used for organ weight data is indicated in the data-tables, and were sufficient for statistical analysis.
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
Metric 20:	Negative Control Response	Medium	There was no indication in the text that results from control groups were unexpected. Responses of controls used for histopathology were not reported.
Variable Cor	ntrol		
Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant
	Contin	ued on next pa	age
	Metric 11:  Metric 12:  Metric 13:  Metric 14:  Metric 15:  Ssment Metric 16: Metric 17:  Metric 19: Metric 20:  Variable Con Metric 21:  Metric 22:	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Number of Animals per Group  Metric 15: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method Low  Metric 13: Test Animal Characteristics Low  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group Medium  Sisment  Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment Low  Metric 18: Sampling Adequacy Medium  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response Medium  Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Health Outcomes Unrelated to Medium  Exposure

HERO ID: 62617 Table: 10 of 18

1,1-Dichloroethane

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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Cardiovascular (This form is for Guinea pigs)

Outcome(s): Reported Health

Gross examinations; histology; organ weights

Effect(s):

**Duration:** Chronic (>91 days) Chronic; Guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Low	Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability for the mid exposure level only. Incidences of histopathology were not reported.

# Overall Quality Determination Medium

Study Citation:	Spencer H.C. Rowe V.K. Adams F.M. Mccollister D.	D. Irish D.D. (1951)	Vapor toxicity of ethylene dichloride determined by experiments on			
Study Citation.	laboratory animals. Archives of Industrial Hygiene and Occ					
Health	Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);					
Outcome(s):		•				
Reported Health	Reproductive/Developmental (This form is for rats): Testes:	Gross examinations; h	istology; organ weights; Reproductive/Developmental (This form is for			
Effect(s):	Guinea pigs): Testes: Gross examinations; histology; organ	weights;				
<b>Duration:</b>	Chronic (>91 days) Chronic; rats					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	62617					
Domain	Matria	Dating	Commants			

Domain		Metric	Rating	Comments	
Domain 1: Test Substar	ice				
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided	
	Metric 2:	Test Substance Source	High	All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.	
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.	
Domain 2: Test Design					
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.	
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type	
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.	
Domain 3: Exposure Cl	naracterization				
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.	
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.	
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.	
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Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Reproductive/Developmental (This form is for rats): Testes: Gross examinations; histology; organ weights; Reproductive/Developmental (This form is for

Health Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);

Outcome(s): Reported Health

ntrome(s).

**Effect(s):** Guinea pigs): Testes: Gross examinations; histology; organ weights;

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

HERO ID:	62617			
Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	Low	Reproductive/Developmental (This form is for rats): Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups); Reproductive/Developmental (This form is for Guinea pigs): Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥170 days. At the high exposure level, all of the animals died, so at this level, the overall duration was shorter than expected (32 days for females and 14 days for males). At the mid-exposure level, animals "tolerated" exposure for 246 days, and at the low exposure level, males went 170 days and females went 226 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Reproductive/Developmental (This form is for rats): Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days for females and 56 days for males); this exposure level could therefore note be used to evaluate chronic effects.; Reproductive/Developmental (This form is for Guinea pigs): Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying; this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	Reproductive/Developmental (This form is for rats): The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.; Reproductive/Developmental (This form is for Guinea pigs): Animals were obtained from a commercial source (not specified); however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to reporting animal diets. No other data were provided.
		Continu	ed on next p	age

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
Health	Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);

**Outcome(s):** 

Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);

**Reported Health** 

Reproductive/Developmental (This form is for rats): Testes: Gross examinations; histology; organ weights; Reproductive/Developmental (This form is for

Guinea pigs): Testes: Gross examinations; histology; organ weights; Effect(s):

Chronic (>91 days) Chronic; rats **Duration:** 

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID: 62617

HERO ID:	62617			
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	Reproductive/Developmental (This form is for rats): For exposure groups, animal numbers consisted of 15 rats/sex/group; 20/sex/group is considered appropriate for a chronic study.; Reproductive/Developmental (This form is for Guinea pigs): For exposure groups, animal numbers consisted of 8s/sex/group; 20/sex/group is considered appropriate for a chronic study.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Details of methods relevant to this organ/system were adequately described.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
	Metric 18:	Sampling Adequacy	Medium	Reproductive/Developmental (This form is for rats): For organ weights, the methods do not specifically indicate how many animals were assessed per group, but the numbers evaluated are reported in data tables for the mid-exposure group, and these numbers were sufficient for the outcome of interest. The sampling adequacy for other exposure groups, or for histopathology is not clear, but methods indicate tissues were collected from all animals.; Reproductive/Developmental (This form is for Guinea pigs): For organ weights, the methods do not specifically indicate how many animals were assessed per group, but the numbers evaluated are reported in data tables and these numbers were sufficient for the outcome of interest. The sampling adequacy for histopathology is not clear, but methods indicate tissues were collected from all animals.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Medium	All Outcomes: Details of the biological responses of controls were not specifically discussed. There was no indication in the data tables that results from control groups were unexpected.
Domain 6: Confoundi	ing / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.

HERO ID: 62617 Table: 11 of 18

### ... continued from previous page

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);

**Outcome(s):** 

**Reported Health** Reproductive/Developmental (This form is for rats): Testes: Gross examinations; histology; organ weights; Reproductive/Developmental (This form is for

**Effect(s):** Guinea pigs): Testes: Gross examinations; histology; organ weights;

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	Low	Reproductive/Developmental (This form is for rats): The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant. However, the only data table available at the mid-exposure level does not indicate a statistical test was performed.; Reproductive/Developmental (This form is for Guinea pigs): The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant.
	Metric 24:	Reporting of Data	Low	Reproductive/Developmental (This form is for rats): Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability for the mid exposure level only. The text reported no adverse histological changes were observed, but the data were not provided. The results descriptions only reported comparison with "control values," but does not specify which control group was used for comparisons.; Reproductive/Developmental (This form is for Guinea pigs): Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability. Results do not include the air-only control for low exposure males (no explanation provided). The text reported no adverse histological changes were observed, but the data were not provided.

## **Overall Quality Determination**

## Medium

Human Health Hazard Animal Toxicology Evaluation HERO ID: 62617 Table: 12 of 18

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Immune/Hematological (This form is for rats)

**Outcome(s): Reported Health** 

Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig	on			
Johnan 2. Test Desig	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g. test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and its concurrent air-control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The exact study durations are not clearly stated, but at levels where animals did not die, exposures were ≥198 days. At the high exposure level, all of the animals died, so the overall duration was shorter than expected (10 days for females and 56 days for males). At the mid-exposure level, animals "tolerated" exposure for 212 days, and at the low exposure level, males went 211 days and females went 198 days without showing adverse effects, but it is not clear when exposure was stopped (or if the duration was equivalent between sexes and groups)

Continued on next page ...

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Immune/Hematological (This form is for rats)

Outcome(s):

**Reported Health** Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.

Effect(s):

**Duration:** Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	62617	bethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Not including controls, there were 3 exposure groups. Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying; this exposure level could therefore note be used to evaluate chronic effects.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate and the number of air changes/minute were not reported.
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Low	The source of albino rats was reported; however, the animal strain, age, or starting body weights were not provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting animal diets. No other data were provided.
	Metric 15:	Number of Animals per Group	Medium	For exposure groups, animal numbers consisted of 15 rats/sex/group; 20/sex/group is considered appropriate for a chronic study.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Methods for endpoint-related serum chemistry were not clearly reported. The methods indicate "in many cases" blood was collected at the time of autopsy. Therefore, numbers and groups in which samples were collected is not clear.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between an exposure group (single sex at a specific exposure level) and the concurrent air-only controls for those animals were consistently assessed. Due to the uncertainty of the exact day of exposure termination, it is unclear whether animals across groups (or even sex at the low exposure level) were consistently evaluated.
	Metric 18:	Sampling Adequacy	Medium	For organ weights, the methods do not specifically indicate how many animals were assessed per group. From the data table shown for the mid-exposure level, at least 9 exposed and 11 control animal organ weights were measured, which is sufficient for the outcome of interest. The number of animals used for serum chemistry or hematology is not reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Low	Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g, hematology, histology) because no data were provided. There was no indication in the text that results from control groups were unexpected.
Domain 6: Confounding	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.
			ued on next pa	nge

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Immune/Hematological (This form is for rats)

Outcome(s):

Reported Health

Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.

Effect(s):

Duration: Chronic (>91 days) Chronic; rats

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
	Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant; however, there is no indication that statistical analysis was performed on organ weight measurements in the data table provided.
	Metric 24:	Reporting of Data	Low	Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability for the mid exposure level only. Results for measurement of prothrombin clotting time and hematological measurements were described as non-adverse in the text.

## **Overall Quality Determination**

## Medium

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493. Hepatic/Liver (This form is for Guinea pigs)

Health

**Outcome(s):** Reported Health

Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol

Effect(s):

Chronic (>91 days) Chronic; Guinea pigs **Duration: Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig				
Domain 2: Test Desig	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Di 2. E	Cl			
Domain 3: Exposure		D 4: 164 CT 4	т	
	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups, but there WAS consistency between a single-sex and one exposure level, and the concurrent control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The study duration is not clearly reported and may have varied across groups and between sexes.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days). Not including controls, there were 3 exposure groups for rats and guinea pigs, and 2 exposure groups for rabbits and monkeys.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported.

Domain 4: Test Animals

Continued on next page ...

Iaboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.   Hepatic/Liver (This form is for Guinea pigs)			continu	ied from previ	ous page				
Reported Health Effect(s):  Duration: Chronic (>91 days) Chronic; Guinea pigs Chemical: 1,1-Dichloroethane- Issomer: 1,2-Dichloroethane HRRO ID: C6217  Domain Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group  Husbandry Conditions  Metric 15: Number of Animals per Group  Domain 5: Outcome Assessment  Metric 16: Outcome Assessment  Metric 17: Consistency of Outcome Assessment Methodology  Metric 18: Sampling Adequacy  Metric 18: Sampling Adequacy  Metric 18: Sampling Adequacy  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Low  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Low  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Low  Domain 6: Confounding / Variable Control  Metric 21: No confounding Variables in Test Design  Mediting Variables were reported.  Metric 21: No confounding Variables in Test Design  Mediting Variables were reported.  Metric 21: No confounding Variables in Test Design  Mediting Variables were reported.	Study Citation: Health	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.							
Domain   Chronic (>>91 days) Chronic; Guinea pigs	Outcome(s): Reported Health Effect(s):	Gross exami	Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol						
Metric 13: Test Animal Characteristics    Low	Duration: Chemical: HERO ID:	1,1-Dichloro							
Domain 5: Outcome Assessment  Metric 16: Outcome Assessment  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 18: Sampling Adequacy  Metric 19: Metric 20: Negative Control Response  Low Domain 6: Confounding / Variable Control Metric 21: Confounding Variables in Test Design Medium  No confounding variables were reported.  Medium No confounding variables were reported.  Medium No confounding variables were reported. Medium No confounding variables were reported.  Medium No confounding variables were reported.  Medium No confounding variables were reported.  Medium No confounding variables were reported.	Domain		Metric	Rating	Comments				
Husbandry Conditions Metric 15: Number of Animals per Group  Low For exposure groups, animal numbers consisted of 15-20 rats/sex/group; 8 guinea pigs/sex/group; 2 male and 1 female rabbit/group, and 2 male monkeys/ group. The text reports that numbers in control groups were meant to match numbers in exposure groups. OECD guidance indicates 20 animals per sex should be used in a chronic study in rodents.  Domain 5: Outcome Assessment  Metric 16: Outcome Assessment Methodology Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Medium  Metric 18: Sampling Adequacy  Medium  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Low  Domain 6: Confounding / Variable Control  Metric 20: Confounding Variables in Test Design  Medium  No confounding variables were reported.		Metric 13:	Test Animal Characteristics	Low	ported to come from commercial sources, however, with the exception of rats, the specific sources were not reported. No details on animal strain, age, or starting body				
pigysex/group; 2 male and 1 female rabbit/group, and 2 male monkeys/ group. The text reports that numbers in control groups were meant to match numbers in exposure groups. OECD guidance indicates 20 animals per sex should be used in a chronic study in rodents.  Domain 5: Outcome Assessment  Metric 16: Outcome Assessment Methodology High Details of methods relevant to this organ/system were appropriately described.  Metric 17: Consistency of Outcome Assessment Low Outcomes between a single treated sex at a single exposure level, and that group's concurrent control were consistently assessed. It is unclear whether outcomes were assessed consistently across groups, or between sexes due to the uncertainties of whether exposure durations from each group or sex were equivalent.  Metric 18: Sampling Adequacy Medium Specific details regarding sampling of outcomes were clearly reported for some, but not all endpoints. For example, the text indicates that "in many cases" blood was collected at the time of autopsy, and "in many cases" aportion of the liver was frozen for lipid analysis. However, for histopathology, the text indicates that "all survivors were examined for evidence of organic injury."  Metric 20: Negative Control Response  Negative Control Response  Low Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g., hematology, histology). In some cases data for only the unexposed controls was provided, and therefore it is unclear whether responses from the air-only controls was appropriate. Under cricumstances where control response day were provided (e.g., some organ weight data, and some body weight data), the responses appear to be appropriate.  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.		Metric 14:		Low	, , , , , , , , , , , , , , , , , , , ,				
Metric 16: Outcome Assessment Methodology Metric 17: Consistency of Outcome Assessment  Low Outcomes between a single treated sex at a single exposure level, and that group's concurrent control were consistently assessed. It is unclear whether outcomes were assessed consistently across groups, or between sexes due to the uncertainties of whether exposure durations from each group or sex were equivalent.  Metric 18: Sampling Adequacy  Medium Metric 19: Blinding of Assessors Metric 20: Negative Control Response  Low Details of methods relevant to this organ/system were appropriately described.  Metric 18: Sampling Adequacy  Medium Medium Specific details regarding sampling of outcomes were clearly reported for some, but not all endpoints. For example, the text indicates that "in many cases" blood was collected at the time of autopsy, and "in many cases" a portion of the liver was frozen for lipid analysis. However, for histopathology, the text indicates that "all survivors were examined for evidence of organic injury."  Metric 20: Negative Control Response  Low Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g., hematology, histology). In some cases data for only the unexposed controls was provided, and therefore it is unclear whether responses from the air-only controls was appropriate. Under circumstances where control response data were provided (e.g., some organ weight data, and some body weight data), the responses appear to be appropriate.  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.		Metric 15:	Number of Animals per Group	Low	pigs/sex/group; 2 male and 1 female rabbit/group, and 2 male monkeys/ group. The text reports that numbers in control groups were meant to match numbers in exposure groups. OECD guidance indicates 20 animals per sex should be used in a chronic study				
Metric 17: Consistency of Outcome Assessment  Low Outcomes between a single treated ex at a single exposure level, and that group's concurrent control were consistently assessed. It is unclear whether outcomes were assessed consistently across groups, or between sexes due to the uncertainties of whether exposure durations from each group or sex were equivalent.  Metric 18: Sampling Adequacy  Medium  Specific details regarding sampling of outcomes were clearly reported for some, but not all endpoints. For example, the text indicates that "in many cases" blood was collected at the time of autopsy, and "in many cases" a portion of the liver was frozen for lipid analysis. However, for histopathology, the text indicates that "all survivors were examined for evidence of organic injury."  Metric 19: Blinding of Assessors  N/A  Metric 20: Negative Control Response  Low  Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g., hematology, histology). In some cases data for only the unexposed controls was provided, and therefore it is unclear whether responses from the air-only controls was appropriate. Under circumstances where control response data were provided (e.g., some organ weight data, and some body weight data), the responses appear to be appropriate.  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design  Medium  No confounding variables were reported.	Domain 5: Outcome	Assessment							
Current control were consistently assessed. It is unclear whether outcomes were assessed consistently aross groups, or between sexes due to the uncertainties of whether exposure durations from each group or sex were equivalent.  Metric 18: Sampling Adequacy  Medium  Medium  Specific details regarding sampling of outcomes were clearly reported for some, but not all endpoints. For example, the text indicates that "in many cases" blood was collected at the time of autopsy, and "in many cases" a portion of the liver was frozen for lipid analysis. However, for histopathology, the text indicates that "all survivors were examined for evidence of organic injury."  Metric 19: Blinding of Assessors  N/A  Blinding was not necessary for the outcomes assessed.  Metric 20: Negative Control Response  Low  Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g., hematology, histology). In some cases data for only the unexposed controls was appropriate. Under circumstances where control response data were provided (e.g., some organ weight data, and some body weight data), the responses appear to be appropriate.  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design  Medium  No confounding variables were reported.			23	-					
not all endpoints. For example, the text indicates that "in many cases" blood was collected at the time of autopsy, and "in many cases" a portion of the liver was frozen for lipid analysis. However, for histopathology, the text indicates that "all survivors were examined for evidence of organic injury."  Metric 19: Blinding of Assessors N/A Blinding was not necessary for the outcomes assessed.  Metric 20: Negative Control Response Low Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g., hematology, histology). In some cases data for only the unexposed controls was provided, and therefore it is unclear whether responses from the air-only controls was appropriate. Under circumstances where control response data were provided (e.g., some organ weight data, and some body weight data), the responses appear to be appropriate.  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  and Procedures		Metric 17:	Consistency of Outcome Assessment	Low	current control were consistently assessed. It is unclear whether outcomes were assessed consistently across groups, or between sexes due to the uncertainties of whether expo-				
Metric 20: Negative Control Response  Low Details of the biological responses of controls were not provided or were poorly described for some endpoints (e.g., hematology, histology). In some cases data for only the unexposed controls was provided, and therefore it is unclear whether responses from the air-only controls was appropriate. Under circumstances where control response data were provided (e.g., some organ weight data, and some body weight data), the responses appear to be appropriate.  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Medium No confounding variables were reported.		Metric 18:	Sampling Adequacy	Medium	not all endpoints. For example, the text indicates that "in many cases" blood was collected at the time of autopsy, and "in many cases" a portion of the liver was frozen for lipid analysis. However, for histopathology, the text indicates that "all survivors were				
scribed for some endpoints (e.g., hematology, histology). In some cases data for only the unexposed controls was provided, and therefore it is unclear whether responses from the air-only controls was appropriate. Under circumstances where control response data were provided (e.g., some organ weight data, and some body weight data), the responses appear to be appropriate.  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  and Procedures		Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the outcomes assessed.				
Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  and Procedures		Metric 20:	Negative Control Response	Low	scribed for some endpoints (e.g, hematology, histology). In some cases data for only the unexposed controls was provided, and therefore it is unclear whether responses from the air-only controls was appropriate. Under circumstances where control response data were provided (e.g., some organ weight data, and some body weight data), the responses				
Metric 21: Confounding Variables in Test Design Medium No confounding variables were reported.  and Procedures	Domain 6: Confound	ing / Variable Co	ntrol						
Continued on next page		-	Confounding Variables in Test Design	Medium	No confounding variables were reported.				
			Continu	ued on next pa	nge				

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Hepatic/Liver (This form is for Guinea pigs)

Outcome(s):

Reported Health

Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol

Effect(s):

**Duration:**Chronic (>91 days) Chronic; Guinea pigs**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study. It is unclear, what was meant by animals "tolerating" exposure. Exposure durations of some animals were "tolerated" longer than others. It is unclear whether groups of animals exposed for shorter durations were showing signs of toxicity or "lack of tolerance" and therefore the exposures were stopped sooner? Since no comparisons were done across exposures this is not likely to have an impact on the study results.
	Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls whre relevant.
	Metric 24:	Reporting of Data	Low	Quantal data was provided for body weights and relative organ weights only (reported as means in the absence of measures of variability; in only some study groups for rats and guinea pigs only). In some cases, (e.g., histological examinations) comparisons were inappropriately done with the unexposed control groups (no comparisons with the air-only controls were described). In other cases, it is unclear which control groups were used for comparisons since the descriptions only indicate "controls".

## **Overall Quality Determination**

## Medium

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
Health	Neurological/Behavioral (This form is for Guinea pigs); Neurological/Behavioral (This form is for Rats);

Outcome(s): Reported Health

Neurological/Behavioral (This form is for Guinea pigs): Clinical signs; Neurological/Behavioral (This form is for Rats): Clinical signs;

Effect(s):

**Duration:**Chronic (>91 days) Chronic; Guinea pigs**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
Metr	ric 1:	Test Substance Identity	High	All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
Metr	ric 2:	Test Substance Source	High	All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
Metr	ric 3:	Test Substance Purity	High	All Outcomes: Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design				
Metr	ric 4:	Negative and Vehicle Controls	High	All Outcomes: The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
Metr	ric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
Metr	ric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure Character	rization			
Metr		Preparation and Storage of Test Substance	Low	All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
Metr		Consistency of Exposure Administration	Low	All Outcomes: Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups, but there WAS consistency between a single-sex and one exposure level, and the concurrent control group.
Metr	ric 9:	Reporting of Doses/Concentrations	High	All Outcomes: All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
Metr	ric 10:	Exposure Frequency and Duration	Low	All Outcomes: Animals were exposed 7hrs/day; 5 days/week. The study duration is not clearly reported and may have varied across groups and between sexes.
Metr		Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying within 14 days. Not including controls, there were 3 exposure groups for rats and guinea pigs, and 2 exposure groups for rabbits and monkeys.

		contin	ued from p	revious page				
Study Citation: Health	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments or laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493. Neurological/Behavioral (This form is for Guinea pigs); Neurological/Behavioral (This form is for Rats);							
	Neurological/Benavioral (This form is for Guinea pigs); Neurological/Benavioral (This form is for Rats);							
Outcome(s):	NI1:1	//D-1i1 (TLi- f i- f Cii)	Cl::1 .:.	Normala di al/Dala di anal /Thia farma in fara Data). Climinal di ana				
Reported Health	Neurologica	/Benavioral (This form is for Guinea pigs):	Clinical sig	ens; Neurological/Behavioral (This form is for Rats): Clinical signs;				
Effect(s):	CI : (> 0	1.1. \ 0						
Duration:		1 days) Chronic; Guinea pigs						
Chemical:	*	ethane- Isomer: 1,2-Dichloroethane						
HERO ID:	62617							
Domain	15 1 16	Metric	Rating	Comments				
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported.				
Domain 4: Test Animals								
	Metric 13:	Test Animal Characteristics	Low	All Outcomes: A number of species were used (rat, guinea pig, rabbit, and monkey); most were reported to come from commercial sources, however, with the exception of rats, the specific sources were not reported. No details on animal strain, age, or starting body weights were provided. The text indicates both sexes were used.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to reporting the diets provided. No other data were provided.				
	Metric 15:	Number of Animals per Group	Low	All Outcomes: For exposure groups, animal numbers consisted of 15-20 rats/sex/group, 8 guinea pigs/sex/group; 2 male and 1 female rabbit/group, and 2 male monkeys/ group. The text reports that numbers in control groups were meant to match numbers in exposure groups. OECD guidance indicates 20 animals per sex should be used in a chronic study in rodents.				
Domain 5: Outcome Asse								
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The text indicates animals were "observed frequently" for general appearance and behavior but no further details were provided.				
	Metric 17:	Consistency of Outcome Assessment	Medium	Neurological/Behavioral (This form is for Guinea pigs): Outcomes between a single treated sex at a single exposure level, and that group's concurrent control were consistently assessed. It is unclear whether outcomes were assessed consistently across groups, or between sexes due to the uncertainties of whether exposure durations from each group or sex were equivalent. had For example, at 200 ppm, it was reported that guinea pigs "tolerated" 180 exposures in 246 days, while at 100 ppm, males "tolerated" 121 exposures in 170 days and females 162 exposures in 226 days. This is not likely to have a large impact on behavioral observations.; Neurological/Behavioral (This form is for Rats): Outcomes between a single treated sex at a single exposure level, and that group's concurrent control were consistently assessed. It is unclear whether outcomes were assessed consistently across groups, or between sexes due to the uncertainties of whether exposure durations from each group or sex were equivalent.				
	Metric 18:	Sampling Adequacy	High	All Outcomes: Study methods indicate that EACH animal was observed.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary for this outcome				
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological responses of controls for this endpoint were not reported.				
Domain 6: Confounding	/ Variable Co	atrol						
Domain o. Comounting	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.				

Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
-	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
Health	Neurological/Behavioral (This form is for Guinea pigs); Neurological/Behavioral (This form is for Rats);
Outcome(s):	

Reported Health

Neurological/Behavioral (This form is for Guinea pigs): Clinical signs; Neurological/Behavioral (This form is for Rats): Clinical signs;

Effect(s):

**Duration:** Chronic (>91 days) Chronic; Guinea pigs **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information on health outcomes unrelated to exposure were reported.  All animals were reported to be healthy at the start of the study. It is unclear, what was meant by animals "tolerating" exposure. Exposure durations of some animals were "tolerated" longer than others. It is concerning that perhaps some groups were showing signs of toxicity and therefore the exposures were stopped sooner? Since no comparisons were done across exposures this is not likely to have an impact on the study results.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls where relevant.
	Metric 24:	Reporting of Data	Low	All Outcomes: The text qualitatively indicated that severe intoxication was reported in the highest exposure groups. Incidences or specific results per sex were not provided. This endpoint is not mentioned in results sections for the mid and low exposure groups

# Overall Quality Determination High

HERO ID: 62617 Table: 15 of 18 1,1-Dichloroethane

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Neurological/Behavioral Health

**Outcome(s):** 

**Reported Health** Clinical signs

Effect(s):

Chronic (>91 days) Chronic; Monkey **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 62617

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Desig	n			
	Metric 4:	Negative and Vehicle Controls	High	The study included both unexposed and air-exposed controls. Note* There were separate concurrent controls for each sex at each exposure level.
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure 0	Characterization			
-	Metric 7:	Preparation and Storage of Test Substance	Low	Equipment used for vapor generation was described, but some details were missing (e.g. test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Low	Different chambers were used for different exposure groups. A 450-L capacity was used for the mid-exposure group, and a 1,700-liters box was used for the two other exposure groups. However, concurrent air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Overall, there was a lack of consistency across groups and between sexes, but there WAS consistency between a single-sex and one exposure level, and the concurrent control group.
	Metric 9:	Reporting of Doses/Concentrations	High	All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Low	Animals were exposed 7hrs/day; 5 days/week. The study duration varied across groups and between sexes. It is unclear if this was part of the study design. No explanations were provided.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic with a significant number of animals dying (100% mortality within 14 days). Not including controls, there were 3 exposure groups for rats and guinea pigs, and 2 exposure groups for rabbits and monkeys.
	Metric 12:	Exposure Route and Method	Low	Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported.

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Neurological/Behavioral

**Outcome(s):** 

**Reported Health** 

Clinical signs

Effect(s):

Chronic (>91 days) Chronic; Monkey **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

HERO ID.	02017			
Domain		Metric	Rating	Comments
Domain 4: Test Anima	ls			
	Metric 13:	Test Animal Characteristics	Low	A number of species were used (rat, guinea pig, rabbit, and monkey); most were reported to come from commercial sources, however, with the exception of rats, the specific sources were not reported. No details on animal strain, age, or starting body weights were provided. The text indicates both sexes were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry information was limited to reporting the diets provided. No other data were provided.
	Metric 15:	Number of Animals per Group	Medium	For exposure groups, animal numbers consisted of 15-20 rats/sex/group; 8 guinea pigs/sex/group; 2 male and 1 female rabbit/group, and 2 male monkeys/ group. The text reports that numbers in control groups were meant to match numbers in exposure groups. Since this is not a carcinogenicity study, in general, the numbers are appropriate
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	The text indicates animals were "observed frequently" for general appearance and behavior but no further details were provided.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcomes between a single treated sex at a single exposure level, and that group's concurrent control were consistently assessed. Outcomes; however, were not assessed consistently across groups, or between sexes. For example, at 200 ppm, it was reported that guinea pigs "tolerated" 180 exposures in 246 days, while at 100 ppm, males "tolerated" 121 exposures in 170 days and females 162 exposures in 226 days. Therefore, in the latter example, emdpoints from males and females from the same exposure group were evaluated at different times.
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome
	Metric 20:	Negative Control Response	High	The biological responses of controls (that were reported) appeared to be appropriate.
Domain 6: Confoundin	ng / Variable Cor	ntrol		
o, comounding	Metric 21:	Confounding Variables in Test Design	Medium	No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to	Medium	No information on health outcomes unrelated to exposure were reported. All animals
		Exposure		were reported to be healthy at the start of the study. It is unclear, what was meant by animals "tolerating" exposure. Exposure durations of some animals were "tolerated" longer than others. It is concerning that perhaps some groups were showing signs of toxicity and therefore the exposures were stopped sooner? Since no comparisons were done across exposures this is not likely to have an impact on the study results.
	Metric 23:	Data Presentation and Analysis	High	The text indicates that T-tests were performed comparing exposed groups to air-exposed

1,1-Dichloroethane

... continued from previous page

HERO ID: 62617 Table: 15 of 18

Study Citation: Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on

laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

**Health** Neurological/Behavioral

**Outcome(s):** 

Reported Health

Clinical signs

**Effect(s):** 

**Duration:** Chronic (>91 days) Chronic; Monkey

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	Medium	The text qualitatively indicated that in most cases, no behavioral changes were observed. Severe intoxication was reported in the highest exposure groups. The summary does not specifically say whether control rats appeared normal.

Overall Quality Determination High

Study Citation:				1). Vapor toxicity of ethylene dichloride determined by experiments on					
TT 1/1		animals. Archives of Industrial Hygiene and Oc							
Health		Neurological/Behavioral (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Nutritional/Metabolic (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Hangier (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Hangier (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Hangier (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Nutritional/Metabolic (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Nutritional/Metabolic (This form is for Rabbit							
Outcome(s):	Rabbits); Immune/Hematological (This form is for Rabbits); Renal/Kidney (This form is for Rabbits); Hepatic/Liver (This form is for Rabbits); Lung/Respiratory (This form is for Rabbits); Cardiovascular (This form is for Rabbits);								
Reported Health				abbits); e/Developmental (This form is for Rabbits): Testes: Gross examinations;					
Effect(s):				by weight; food consumption; Immune/Hematological (This form is for					
Lifect(5).				e tissues examined.; Renal/Kidney (This form is for Rabbits): Gross ex-					
				Gross examinations; histology; organ weights; liver lipid analysis; free					
				examinations; histology; organ weights; Cardiovascular (This form is for					
		ross examinations; histology; organ weights;	, for rancons, Gross	motorogy, organ worging, curate vaccular (11110 form to for					
<b>Duration:</b>		91 days) Chronic; Rabbit							
Chemical:		oethane- Isomer: 1,2-Dichloroethane							
HERO ID:	62617	, , , , , , , , , , , , , , , , , , , ,							
Domain		Metric	Rating	Comments					
Domain 1: Test Substa									
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided					
	Metric 2:	Test Substance Source	High	All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.					
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity ≥99.7 %; the only impurity identified was trichloroethylene.					
Domain 2: Test Design	n								
C	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: The general study methods indicated both unexposed and air-exposed controls were used, but it is unclear if this applied to the studies on rabbits. The results do not reference comparison to any controls.					
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type					
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to groups, however,					
				all animals were reported to be in good health, and controls (if used) were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.					
Domain 3: Exposure (	Characterization								
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.					
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Unexposed controls were kept in a separate room.					
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.					

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			inued from previou					
Study Citation:	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on							
Health		laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.  Neurological/Behavioral (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Nutritional/Metabolic (This form is for						
Outcome(s):	Rabbits); Immune/Hematological (This form is for Rabbits); Renal/Kidney (This form is for Rabbits); Hepatic/Liver (This form is for Rabbits);							
outcome(s).		atory (This form is for Rabbits); Cardiovascular						
Reported Health				ve/Developmental (This form is for Rabbits): Testes: Gross examinations;				
Effect(s):	histology; or	rgan weights; Nutritional/Metabolic (This form	is for Rabbits): Bo	ody weight; food consumption; Immune/Hematological (This form is for				
				e tissues examined.; Renal/Kidney (This form is for Rabbits): Gross ex-				
				: Gross examinations; histology; organ weights; liver lipid analysis; free				
			for Rabbits): Gross	examinations; histology; organ weights; Cardiovascular (This form is for				
Duration:		oss examinations; histology; organ weights; 1 days) Chronic; Rabbit						
Chemical:		bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	62617	retitatie Isolitet. 1,2 Bielitoroctitatie						
Domain		Metric	Rating	Comments				
	Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: Animals were exposed 7hrs/day; 5 days/week. The day of termination is not clearly stated. The text indicates that at the high exposure level, rabbits tolerated 232 exposure days and at the low exposure level they tolerated 248 exposure days, without evidence of adverse effects.				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Justification of the exposure levels was not provided. No adverse effects were observed at either dose level				
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported.				
Domain 4: Test Anim	alc							
Domain 7. Test 7 mini	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Not a preferred species for chronic studies. Rabbits were from a laboratory stock. Other details including strain, age, initial body weights etc., were not provided.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to reporting the diets provided. No other data were provided.				
	Metric 15:	Number of Animals per Group	Low	All Outcomes: Exposure groups consisted of 2 males and 1 female; this is lower than the number of rodents typically included in a chronic study.				
Damain 5: Outcome	A academant			** *				
Domain 5: Outcome A	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: General methods of outcome assessment were described; some details				
	Wietire 10.	outcome ressessment methodology	Wediam	were less clear (e.g., animals were observed "frequently"; "records were kept" of food				
				consumption and mortality, but without indication of the frequency of measurements). Other measurements (body weight, organ weight, histopathology) were reported to be performed on ALL animals.				
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: There is no indication that there were differences in outcome assessmen				
		·		in the two surviving animals. Since control animals (other than in the methods) are not discussed it is difficult to assess consistency.				
	Metric 18:	Sampling Adequacy	Medium	All Outcomes: Sampling outcomes were not reported; it is assumed all 3 animals per group were evaluated.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the outcomes assessed.				
	Metric 20:	Negative Control Response	Low	All Outcomes: Details of the biological responses of controls were not provided.				

**Study Citation:** Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.

Health

Neurological/Behavioral (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Nutritional/Metabolic (This form is for Outcome(s): Rabbits); Immune/Hematological (This form is for Rabbits); Renal/Kidney (This form is for Rabbits); Hepatic/Liver (This form is for Rabbits);

Lung/Respiratory (This form is for Rabbits); Cardiovascular (This form is for Rabbits);

Neurological/Behavioral (This form is for Rabbits): Clinical signs; Reproductive/Developmental (This form is for Rabbits): Testes: Gross examinations; **Reported Health** histology; organ weights; Nutritional/Metabolic (This form is for Rabbits): Body weight; food consumption; Immune/Hematological (This form is for Effect(s):

> Rabbits): Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.; Renal/Kidney (This form is for Rabbits): Gross examinations; histology; organ weights; Hepatic/Liver (This form is for Rabbits): Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Lung/Respiratory (This form is for Rabbits): Gross examinations; histology; organ weights; Cardiovascular (This form is for

Rabbits): Gross examinations; histology; organ weights;

**Duration:** Chronic (>91 days) Chronic; Rabbit

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

62617 **HERO ID:** 

Domain		Metric	Rating	Comments
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
	Metric 23:	Data Presentation and Analysis	Uninformative	All Outcomes: Although the methods indicate that T-tests were performed when possible, the results from experiments with rabbits do not mention or indicate any comparisons to controls were performed.
	Metric 24:	Reporting of Data	Uninformative	All Outcomes: Results in rabbits were insufficiently described, with a general statement that no adverse effects were observed for any of the endpoints evaluated. No data were provided for independent review.

## **Overall Quality Determination**

## Uninformative

Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
Hepatic/Liver (This form is for Monkey); Mortality (This form is for Monkey); Nutritional/Metabolic (This form is for Monkey); Immune/Hematological
(This form is for Monkey); Mortality (This form is for Rabbits); Renal/Kidney (This form is for Monkey);
Hepatic/Liver (This form is for Monkey): Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Mortality
(This form is for Monkey): Death; Nutritional/Metabolic (This form is for Monkey): Body weight; food consumption; Immune/Hematological (This form
is for Monkey): Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.; Mortality (This form is for Rabbits): Death;
Renal/Kidney (This form is for Monkey): Gross examinations; histology; organ weights;
Chronic (>91 days) Chronic; Monkey
1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
62617

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
-	Metric 3:	Test Substance Purity	High	All Outcomes: Purity $\geq$ 99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: The general study methods indicated both unexposed and air-exposed controls were used, but it is unclear if this applied to the studies on Monkeys. The results from Monkey studies do not mention any controls, and hematology results were compared to the monkey's pre-treatment examination values rather than to controls.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls (if used) were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure Ch	naracterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: A 1,700-liters box was used for these exposure groups. Assuming controls were included (however, this is unclear), air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Unexposed controls were kept in a separate room.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Animals were exposed 7hrs/day; 5 days/week. The text suggests that both exposure groups were meant to undergo chronic duration exposures, but due to morbidity, the high exposure level animals were sacrificed early.
		Cont	inued on next pa	nge

Study Citation:		C., Rowe, V.K., Adams, E.M., Mccollister, Inimals. Archives of Industrial Hygiene and O		D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
Health				edicine 4(3):482-493. Onkey); Nutritional/Metabolic (This form is for Monkey); Immune/Hematological
		•		\$77
Outcome(s):	*	s for Monkey); Mortality (This form is for Ra	* *	3.77
Reported Health		• •		gy; organ weights; liver lipid analysis; free and esterified cholesterol; Mortality
Effect(s):	*		•	or Monkey): Body weight; food consumption; Immune/Hematological (This form
				s. Lymph node tissues examined.; Mortality (This form is for Rabbits): Death;
		y (This form is for Monkey): Gross examinat	tions; histology	; organ weights;
Duration:	,	1 days) Chronic; Monkey		
Chemical:		bethane- Isomer: 1,2-Dichloroethane		
HERO ID:	62617			
Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic and animals were sacrificed. The low exposure level reported no effects.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported.
Domain 4: Test Animals	3			
Domain rest rimman	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Rhesus monkeys were reported to be imported (source not specified), and
	Wette 13.	Test Allimai Characteristics	Low	kept in the laboratory for several months before use. No further details on starting body weights, or life-stage were provided. Later in the study, it is indicated that the monkeys were males.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to reporting the diets provided. No other data were provided.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 2 males per exposure group were included. Although the number is low, it is considered acceptable for this species.
Damain 5, Outcome As	a a a a ma a m t			
Domain 5: Outcome As		Outcome Assessment Methodology	Madium	All Outcomes Consol with the feature consoleration described consoleration
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: General methods of outcome assessment were described; some details were less clear (e.g., animals were observed "frequently"; "records were kept" of food consumption and mortality, but without indication of the frequency of measurements). Other measurements (body weight, organ weight, histopathology) were reported to be performed on ALL animals.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: There is no indication that there were differences in outcome assessment in the two surviving animals. Since control animals (other than in the methods) are not discussed it is difficult to assess consistency.
	Metric 18:	Sampling Adequacy	High	All Outcomes: All 4 of the exposed animals were evaluated.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the outcomes assessed.
	Metric 20:	Negative Control Response	Low	All Outcomes: Details of the biological responses of controls were not provided.
	1.101.10 20.		2011	2 2
Domain 6: Confounding			3.6 **	
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.
		EADURINE.		in annual were reported to be ilearnly at the start of the stady.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: NA due to the small sample size

<b>Study Citation:</b>	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on
	laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.
Health	Hepatic/Liver (This form is for Monkey); Mortality (This form is for Monkey); Nutritional/Metabolic (This form is for Monkey); Immune/Hematological

Outcome(s): (This form is for Monkey); Mortality (This form is for Rabbits); Renal/Kidney (This form is for Monkey);

**Reported Health**Hepatic/Liver (This form is for Monkey): Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Mortality (This form is for Monkey): Death; Nutritional/Metabolic (This form is for Monkey): Body weight; food consumption; Immune/Hematological (This form

is for Monkey): Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.; Mortality (This form is for Rabbits): Death;

HERO ID: 62617 Table: 17 of 18

Renal/Kidney (This form is for Monkey): Gross examinations; histology; organ weights;

**Duration:** Chronic (>91 days) Chronic; Monkey

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62617

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	Low	All Outcomes: Effects observed in moribund animals were clearly described. The text indicated that in low-exposure animals, there were no adverse effects observed for any of the endpoints evaluated. Quantal data of means or measured values were not provided.

## Overall Quality Determination Medium

HERO ID: 62617 Table: 18 of 18

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ı	١. ا	-	1)	1C	n	loroethane

Study Citation: Health	laboratory a	nimals. Archives of Industrial Hygiene and Occ	upational Medicine	1). Vapor toxicity of ethylene dichloride determined by experiments on 4(5):482-493.  Monkey); Reproductive/Developmental (This form is for Monkey);
Outcome(s): Reported Health Effect(s): Duration: Chemical: HERO ID:	tions; histolo Chronic (>9			an weights; Lung/Respiratory (This form is for Monkey): Gross examina- Monkey): Testes: Gross examinations; histology; organ weights;
Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified as Ethylene dichloride (1,2-dichloroethane); SMILES and pchem properties provided
	Metric 2:	Test Substance Source	High	All Outcomes: 4 individual samples from a commercial source were used (source and batch/lot not specified; however, the identity was verified using infrared-absorption spectra.
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity ≥99.7 %; the only impurity identified was trichloroethylene.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: The general study methods indicated both unexposed and air-exposed controls were used, but it is unclear if this applied to the studies on Monkeys. The results from Monkey studies do not mention any controls, and hematology results were compared to the monkey's pre-treatment examination values rather than to controls.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to groups, however, all animals were reported to be in good health, and controls (if used) were reported to be well-matched with experimental animals in respect to number, age, sex, and body weight.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Equipment used for vapor generation was described, but some details were missing (e.g., test substance storage conditions prior to vaporization); the test substance is a volatile chemical, and this could substantially impact results for a long-term study.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: A 1,700-liters box was used for these exposure groups. Assuming controls were included (however, this is unclear), air-only controls were reported to be exposed to air in chambers similar to their respective experimental groups. Unexposed controls were kept in a separate room.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: All vapor concentrations were monitored using a continuously recording analyzer and concentrations were uniformly held within 10% of the desired concentration.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Animals were exposed 7hrs/day; 5 days/week. The text suggests that both exposure groups were meant to undergo chronic duration exposures, but due to morbidity, the high exposure level animals were sacrificed early.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Justification of the exposure levels was not provided. The highest concentration appeared to be extremely toxic and animals were sacrificed. The low exposure level reported no effects.
		Cont	tinued on next page	···

		0	ontinued from previous pa	ge			
Study Citation: Health	laboratory a	Spencer, H.C., Rowe, V.K., Adams, E.M., Mccollister, D.D., Irish, D.D. (1951). Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals. Archives of Industrial Hygiene and Occupational Medicine 4(5):482-493.  Cardiovascular (This form is for Monkey); Lung/Respiratory (This form is for Monkey); Reproductive/Developmental (This form is for Monkey);					
Outcome(s): Reported Health Effect(s): Duration: Chemical:	tions; histolo Chronic (>9 1,1-Dichloro	Cardiovascular (This form is for Monkey): Gross examinations; histology; organ weights; Lung/Respiratory (This form is for Monkey): Gross examinations; histology; organ weights; Reproductive/Developmental (This form is for Monkey): Testes: Gross examinations; histology; organ weights; Chronic (>91 days) Chronic; Monkey 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	62617						
Domain		Metric	Rating	Comments			
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Vapor generation was clearly described; however, the airflow rate, nor the number of air changes/minute were reported.			
Domain 4: Test Animal	ls						
2011411	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Rhesus monkeys were reported to be imported (source not specified), and kept in the laboratory for several months before use. No further details on starting body weights, or life-stage were provided. Later in the study, it is indicated that the monkeys were males.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to reporting the diets provided. No other data were provided.			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 2 males per exposure group were included. Although the number is low, it is considered acceptable for this species.			
Domain 5: Outcome As	ssessment						
Domain S. Gutesine 7.	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: General methods of outcome assessment were described; some details were less clear (e.g., animals were observed "frequently"; "records were kept" of food consumption and mortality, but without indication of the frequency of measurements). Other measurements (body weight, organ weight, histopathology) were reported to be performed on ALL animals.			
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: There is no indication that there were differences in outcome assessment in the two surviving animals. Since control animals (other than in the methods) are not discussed it is difficult to assess consistency.			
	Metric 18:	Sampling Adequacy	High	All Outcomes: All 4 of the exposed animals were evaluated.			
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the outcomes assessed.			
	Metric 20:	Negative Control Response	Low	All Outcomes: Details of the biological responses of controls were not provided.			
Domain 6: Confoundin	g / Variable Co	ntrol					
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: No confounding variables were reported.			
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information on health outcomes unrelated to exposure was reported. All animals were reported to be healthy at the start of the study.			
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: NA due to the small sample size			
	Metric 24:	Reporting of Data	Uninformative	All Outcomes: Results (quantal or as text) were not reported for multiple organ weights.			
Overall Quali	ty Deterr	nination	Uninformative				

HERO ID: 200612 Table: 1 of 6

**Study Citation:** Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293.

Health Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** Tumor incidence (examination of thymus and isolation of individual masses)

Effect(s):

**Duration:** Chronic (>91 days) 40 weeks-Females

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

Domain		Metric	Rating	Comments
Domain 1: Test Substa	nce			
	Metric 1:	Test Substance Identity	High	The test compound was identified as 1,2-dichloroethane
	Metric 2:	Test Substance Source	High	The test substance was purchased from Fisher Scientific.
	Metric 3:	Test Substance Purity	High	The purity was reported to be 99.8%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	An appropriate negative control (corn oil) was used.
	Metric 5:	Positive Controls	Low	Although not stated in the guidelines for a carcinogenesis study, the authors used benzene as a known compound that induces lymphoma in mice. The study duration was significantly shorter compared to OECD carcinogenesis guideline studies so benzene was used to ensure the duration was sufficient in the transgenic mouse model. However, benzene did not show statistically significant increases in the incidence in lymphoma compared to the negative control.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	haracterization Metric 7:	Preparation and Storage of Test Substance	Low	Test substance dosing solutions were prepared weekly in corn oil and refrigerated until use; however, specific details on preparation procedures and storage (e.g., whether or not tightly capped to prevent volatilization) were not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The volume of corn oil used per kg of body weight was not reported. The gavage volumes used were appropriate for administration of the test substance.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	Low	OECD guidelines for carcinogenicity studies state that the duration of the study should 18-24 months. For females, although study duration was only 40 weeks of dosing an increase in tumor incidence was observed, so this metric was rated as acceptable and low.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	There were deficiencies regarding the number of exposure groups and dose spacing. The highest dose was lowered in weeks 1-3 to the lowest dose, resulting in both groups receiving the same dose level for the majority of the study. Also, there was only a high dose group and a low dose group, guidelines state that there should be at least 3 dosing levels.
	Metric 12:	Exposure Route and Method	High	The route of exposure was appropriate for this type of study and for administration of the test substances.

#### Domain 4: Test Animals

Study Citation: Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

Reported Health

Tumor incidence (examination of thymus and isolation of individual masses)

Effect(s):

**Duration:** Chronic (>91 days) 40 weeks-Females

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Medium	There were minor uncertainties in the reporting of test animal characteristics (starting body weight)but these are unlikely to have a substantial impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported and were adequate and similar for all groups Humidity was not reported.
	Metric 15:	Number of Animals per Group	Low	The reported number of animals per study group (27/sex/group) was lower than the typical number used in studies of the same or similar type (e.g., 50/sex/group for roden cancer bioassay).
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	Histopathology of organs from surviving animals at terminal necropsy was limited to the thymus and to possible tumors and other gross or ophthalmic changes, rather than collecting samples from all tissues typically collected in a study of this type.
	Metric 17:	Consistency of Outcome Assessment	Low	There was incomplete reporting of minor details for the outcome assessment (e.g., timing of collection of tissues from different groups following unscheduled death or the last dose after scheduled necropsy) for histopathology. The duration of the study was reported to be 40 weeks, but the dose was not administered for two weeks due to significant changes in body weight. It is not clear if the total time for the high dose group was 40 weeks with or without the break so it's not clear if the outcomes were measured at the same time points.
	Metric 18:	Sampling Adequacy	Low	Number of animals sampled for tumors and provided in data presented in Figure 2 is no stated so it is unknown if sampling was sufficient.
	Metric 19:	Blinding of Assessors	N/A	It was not necessary to blind assessors
	Metric 20:	Negative Control Response	Low	Due to the high incidence of tumors in the control female transgenic mice, the determination of significant differences between the control and treatment groups was impeded
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups in confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss any differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were adequately described.
	Metric 24:	Reporting of Data	Low	Tumor incidence was reported as the percentage of mice in each treatment group that were found to have malignant lymphoma. The error associated with this calculation was not stated, and the number of animals evaluated was not stated in the text or figure Details of any other analysis was not reported.

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HERO ID: 200612 Table: 1 of 6

1,1-Dichloroethane

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Study Citation: Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293.

Health Cancer/Carcinogenesis

Outcome(s):

**Reported Health** Tumor incidence (examination of thymus and isolation of individual masses)

Effect(s):

**Duration:** Chronic (>91 days) 40 weeks-Females

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

Domain Metric Rating Comments

Overall Quality Determination Medium

Comments

Study Citation: Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** 

Tumor incidence (examination of thymus and isolation of individual masses)

**Effect(s):** 

**Duration:** Chronic (>91 days) 40 weeks-Males

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

HERO ID:	200612			
Domain		Metric	Rating	Comments
Domain 1: Test Substa				
	Metric 1:	Test Substance Identity	High	The test compound was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	The test substance was purchased from Fisher Scientific.
	Metric 3:	Test Substance Purity	High	The purity was reported to be 99.8%
Domain 2: Test Design	1			
C	Metric 4:	Negative and Vehicle Controls	High	An appropriate negative control (corn oil) was used.
	Metric 5:	Positive Controls	Low	Although not stated in the guidelines for a carcinogenesis study, the authors used benzene as a known compound that induces lymphoma in mice. The study duration was significantly shorter compared to OECD carcinogenesis guideline studies so benzene was used to ensure the duration was sufficient in the transgenic mouse model. However, benzene did not show statistically significant increases in the incidence in lymphoma compared to the negative control.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure C	haracterization			
Domain 5. Exposure C	Metric 7:	Preparation and Storage of Test	Low	Test substance dosing solutions were prepared weekly in corn oil and refrigerated until
		Substance		use; however, specific details on preparation procedures and storage (e.g., whether or not tightly capped to prevent volatilization) were not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	The volume of corn oil used per kg of body weight was not reported. The gavage volumes used were appropriate for administration of the test substance.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	Uninformative	For males, study duration was only 40 weeks of dosing and no increase in tumor incidence was observed. OECD guidelines for carcinogenicity studies state that the duration of the study should 18-24 months.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	There were deficiencies regarding the number of exposure groups and dose spacing. The highest dose was lowered in weeks 1-3 to the lowest dose, resulting in both groups receiving the same dose level for the majority of the study. Also, there was only a high dose group and a low dose group, guidelines state that there should be at least 3 dosing levels.
	Metric 12:	Exposure Route and Method	High	The route of exposure was appropriate for this type of study and for administration of the test substances.
Domain 4: Test Anima	ls			
Domain 4. Test Allilla	Metric 13:	Test Animal Characteristics	Medium	There were minor uncertainties in the reporting of test animal characteristics (starting body weight)but these are unlikely to have a substantial impact on results.
		Con	ntinued on next page .	••

Study Citation: Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

Reported Health

Tumor incidence (examination of thymus and isolation of individual masses)

**Effect(s):** 

**Duration:** Chronic (>91 days) 40 weeks-Males

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

HERO ID:	200012			
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported and were adequate and similar for all groups. Humidity was not reported.
	Metric 15:	Number of Animals per Group	Low	The reported number of animals per study group (26 or 27/sex/group) was lower than the typical number used in studies of the same or similar type (e.g., 50/sex/group for rodent cancer bioassay).
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	Histopathology of organs from surviving animals at terminal necropsy was limited to the thymus and to possible tumors and other gross or ophthalmic changes, rather than collecting samples from all tissues typically collected in a study of this type.
	Metric 17:	Consistency of Outcome Assessment	Low	There was incomplete reporting of minor details for the outcome assessment (e.g., timing of collection of tissues from different groups following unscheduled death or the last dose after scheduled necropsy) for histopathology. The duration of the study was reported to be 40 weeks, but the dose was not administered for two weeks due to significant changes in body weight. It is not clear if the total time for the high dose group was 40 weeks with or without the break so it's not clear if the outcomes were measured at the same time points.
	Metric 18:	Sampling Adequacy	Low	Number of animals sampled for tumors and provided in data presented in Figure 2 is not stated so it is unknown if sampling was sufficient.
	Metric 19:	Blinding of Assessors	N/A	Blinding of assessors was not needed.
	Metric 20:	Negative Control Response	Medium	There was incidence of malignant lymphoma in male control mice, but this was not observed in the treatment groups.
Domain 6: Confoun	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups in confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analyses were adequately described.
	Metric 24:	Reporting of Data	Low	Tumor incidence was reported as the percentage of mice in each treatment group that were found to have malignant lymphoma. The error associated with this calculation was not stated, and the number of animals evaluated was not stated in the text or figure. Details of any other analysis was not reported.

## **Overall Quality Determination**

## Uninformative

HERO ID: 200612 Table: 3 of 6

	-	Nichols, W.W	. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM
•			
minune/He	matological, minune/Hematological,		
Immuna/Ha	matalogical: Massurament of packed call vol	uma: hamoglo	hin/magn cornuscular hamoglohin concentration; platelets; hamotocrit; leukocyte
•		, platelets, lien	natocrit, leukocyte, and erythrocyte counts. Thistopathological changes to thymus,
200612	, , , , , , , , , , , , , , , , , , , ,		
	Metric	Rating	Comments
ce			
Metric 1:	Test Substance Identity	High	Immune/Hematological: The test compound was identified as 1,2-dichloroethane; Immune/Hematological: The test compound was identified as 1,2-dichloroethane.
Metric 2:	Test Substance Source	High	All Outcomes: The test substance was purchased from Fisher Scientific.
Metric 3:	Test Substance Purity	High	Immune/Hematological: The purity was reported to be 99.8%; Immune/Hematological: The purity was reported to be 99.8%.
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: An appropriate negative control (corn oil) was used.
	9	~	Immune/Hematological: A positive control was not needed for this study.; Im-
			mune/Hematological: A positive control is not needed for this study.
Metric 6:	Randomized Allocation of Animals	Low	Immune/Hematological: The study did not report how animals were allocated to study groups; Immune/Hematological: The study did not report how animals were allocated to study groups.
orooterization			
	Preparation and Storage of Test	Low	All Outcomes: Test substance dosing solutions were prepared weekly in corn oil and
Wietrie 7.	Substance	Low	refrigerated until use; however, specific details on preparation procedures and storage (e.g., whether or not tightly capped to prevent volatilization) were not reported.
Metric 8:	Consistency of Exposure	Medium	All Outcomes: The volume of corn oil used per kg of body weight was not reported. The
	Administration		gavage volumes used were appropriate for administration of the test substance.
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The animals were administered the dose via gavage daily.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: There were deficiencies regarding the number of exposure groups and dose spacing. The highest dose was lowered in weeks 1-3 to the lowest dose, resulting in
Matri - 12	Evenous Douts and M-41-1	113-1-	both groups receiving the same dose level for the majority of the study.
Metric 12:	Exposure Route and Method	Hign	All Outcomes: The exposure route was acceptable for the administration of a volatile compound.
Metric 13:	Test Animal Characteristics	Medium	All Outcomes: There were minor uncertainties in the reporting of test animal characteristics (starting body weight)but these are unlikely to have a substantial impact on results.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported and were adequate and similar for all groups. Humidity was not reported.
	Contin	ued on next pa	nge
	transgenic n Immune/He Immune/He and erythron hemoglobin, spleen, and chronic (>9 1,1-Dichlore 200612  The Metric 1: Metric 2: Metric 3:  Metric 4: Metric 5: Metric 6:  Metric 6:  Metric 7:  Metric 8: Metric 9: Metric 10: Metric 11:  Metric 12:	transgenic mice. Carcinogenesis 16(2):285-293. Immune/Hematological; Immune/Hematological; Immune/Hematological: Measurement of packed cell vol and erythrocyte counts. Histopathological changes to thy hemoglobin/mean corpuscular hemoglobin concentration spleen, and lymph nodes.; Chronic (>91 days) 40 weeks-Males 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 200612  Metric  Metric 2: Test Substance Identity  Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls  Metric 6: Randomized Allocation of Animals  aracterization  Metric 7: Preparation and Storage of Test Substance  Metric 8: Consistency of Exposure Administration  Metric 9: Reporting of Doses/Concentrations Metric 10: Exposure Frequency and Duration  Metric 11: Number of Exposure Groups and Dose/Concentration Spacing  Metric 12: Exposure Route and Method  Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	transgenic mice. Carcinogenesis 16(2):285-293.  Immune/Hematological; Immune/Hematological;  Immune/Hematological: Measurement of packed cell volume; hemoglob and erythrocyte counts. Histopathological changes to thymus, spleen, a hemoglobin/mean corpuscular hemoglobin concentration; platelets; hem spleen, and lymph nodes.;  Chronic (>91 days) 40 weeks-Males 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 200612  Metric Rating remains and storage of Test Substance Source High Metric 3: Test Substance Purity High Metric 3: Test Substance Purity High Metric 5: Positive Controls N/A Metric 6: Randomized Allocation of Animals Low substance Metric 7: Preparation and Storage of Test Low Substance Metric 9: Reporting of Doses/Concentrations High Metric 10: Exposure Frequency and Duration High Metric 10: Exposure Frequency and Duration High Metric 11: Number of Exposure Groups and Low Dose/Concentration Spacing Metric 12: Exposure Route and Method High Metric 13: Test Animal Characteristics Medium Metric 13: Test Animal Characteristics Medium Metric 14: Adequacy and Consistency of Animal Medium Metric 14: Adequacy and Consistency of Animal Medium

			ied from previ	ous page	
Study Citation:		, Cartwright, M.E., Cook, W.O., Soper, K.A., nice. Carcinogenesis 16(2):285-293.	Nichols, W.W	. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIN	
Health		matological; Immune/Hematological;			
utcome(s):					
Reported Health	Immune/Her	matological: Measurement of packed cell vol	ume; hemoglo	bin/mean corpuscular hemoglobin concentration; platelets; hematocrit; leukocyto	
Effect(s):				and lymph nodes.; Immune/Hematological: Measurement of packed cell volume	
				natocrit; leukocyte, and erythrocyte counts. Histopathological changes to thymus	
	_	ymph nodes.;	, ,	, , ,	
Duration:		01 days) 40 weeks-Males			
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane			
HERO ID:	200612				
Domain		Metric	Rating	Comments	
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals was appropriate for to determine changes to hematology/immune parameters.	
Domain 5: Outcome A	Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Immune/Hematological: Changes to histopathology were assessed for some animal and changes to blood and bone marrow markers were appropriate to assess toxicity.; Immune/Hematological: Changes to histopathology were assessed for some animals ar changes to blood and bone marrow markers were appropriate to assess toxicity.	
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: The duration of the study was reported to be 40 weeks, but the dose was not administered for two weeks due to significant changes in body weight. It is no clear if the total time for the high dose group was 40 weeks with or without the break so it's not clear if the outcomes were measured at the same time points. Changes to histopathology of the thymus, spleen, and lymph nodes was only performed on the animals that died or were terminated prior to the end of the study. The thymus was only examined in mice reaching the end of the study. Hematological parameters were assessed in animals reaching the end of the study and in some cases during early sacrifice	
	Metric 18:	Sampling Adequacy	High	Immune/Hematological: Sampling was appropriate for the paramaters.; Immune/Hematological: Sampling was appropriate for the outcomes of interest.	
	Metric 19:	Blinding of Assessors	N/A	Immune/Hematological: Blinding was not neccessary; Immune/Hematological: Blinding of assessors was not needed for this study.	
	Metric 20:	Negative Control Response	Low	Immune/Hematological: Negative control responses were not reported.; Immune/Hematological: The negative control response was not reported either in tables or texts.	
Domain 6: Confoundi	ing / Variable Co	ntrol			
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confoun- ing, reported information did not identify differences among study groups in confound- ing factors.	
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Immune/Hematological: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcome unrelated to exposure.; Immune/Hematological: There was no information either to support or dismiss any differences among groups in animal attrition or health outcome unrelated to exposure.	
	Metric 23:	Data Presentation and Analysis	High	Immune/Hematological: Statistical methods were adequately described.; Immune/Hematological: Statistical analyses was described appropriately	

Human Health Hazard Animal Toxicology Evaluation HERO ID: 200612 Table: 3 of 6

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**Study Citation:** Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293.

Outcome(s):

Health

Effect(s):

Immune/Hematological; Immune/Hematological;

Reported Health

Immune/Hematological: Measurement of packed cell volume; hemoglobin/mean corpuscular hemoglobin concentration; platelets; hematocrit; leukocyte, and erythrocyte counts. Histopathological changes to thymus, spleen, and lymph nodes.; Immune/Hematological: Measurement of packed cell volume;

hemoglobin/mean corpuscular hemoglobin concentration; platelets; hematocrit; leukocyte, and erythrocyte counts. Histopathological changes to thymus,

spleen, and lymph nodes.;

**Duration:** Chronic (>91 days) 40 weeks-Males

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	Low	All Outcomes: Anemia is reported in text, but tabular results were not provided (e.g., incidence, mean values). All other results were not reported.

#### **Overall Quality Determination** Medium

HERO ID: 200612 Table: 4 of 6

**Study Citation:** Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293. Nutritional/Metabolic; Nutritional/Metabolic;

**Outcome(s):** 

Health

**Reported Health** 

Nutritional/Metabolic: Changes to body weight; Nutritional/Metabolic: Changes to body weight;

Effect(s):

**Duration:** Chronic (>91 days) 40 weeks-Males

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 200612

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	All Outcomes: The test compound was identified as 1,2-dichloroethane
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was purchased from Fisher Scientific.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity was reported to be 99.8%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: An appropriate negative control (corn oil) was used.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control was not needed.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.
Domain 3: Exposure Cl	haracterization			
Zomani or Emposare or	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Test substance dosing solutions were prepared weekly in corn oil and refrigerated until use; however, specific details on preparation procedures and storage (e.g., whether or not tightly capped to prevent volatilization) were not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: The volume of corn oil used per kg of body weight was not reported. The gavage volumes used were appropriate for administration of the test substance.
	Metric 9:	Reporting of Doses/Concentrations	High	Nutritional/Metabolic: Doses were reported without ambiguity.; Nutritional/Metabolic: Doses used were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The animals were administered the dose via gavage daily.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Nutritional/Metabolic: There were deficiencies regarding the number of exposure groups and dose spacing. The highest dose was lowered in weeks 1-3 to the lowest dose, resulting in both groups receiving the same dose level for the majority of the study.; Nutritional/Metabolic: There were deficiencies regarding the number of exposure groups and dose spacing. The highest dose was lowered in weeks 1 to the lowest dose, resulting in both groups receiving the same dose level for the majority of the study.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route was acceptable for the administration of a volatile compound.
Domain 4: Test Animal	s			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: There were minor uncertainties in the reporting of test animal characteristics (starting body weight)but these are unlikely to have a substantial impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported and were adequate and similar for all groups. Humidity was not reported.
	Metric 15:	Number of Animals per Group	Medium	Nutritional/Metabolic: The number of animals was appropriate for the study.; Nutritional/Metabolic: The number of animals was appropriate.

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### Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

**Study Citation:** Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293. Nutritional/Metabolic; Nutritional/Metabolic;

**Outcome(s):** 

Health

**Reported Health** 

Nutritional/Metabolic: Changes to body weight; Nutritional/Metabolic: Changes to body weight;

Effect(s):

Chronic (>91 days) 40 weeks-Males **Duration:** 

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

iieko ib.				
Domain		Metric	Rating	Comments
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	Nutritional/Metabolic: The change in body weight was sufficient to evaluate the outcome of interest.; Nutritional/Metabolic: The methodology was sensitive to measure changes in body weight.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: The same protocol was used to determine changes to body weight over the course of the experiment for all study groups. However, timing of the initial body weight measurement was not explicitly reported. Also, dosing for the high dose group had to be suspended. The duration of the study was reported to be 40 weeks, but the dose was not administered for two weeks due to significant changes in body weight. It is not clear if the total time for the high dose group was 40 weeks with or without the break so it's not clear if the outcomes were measured at the same time points.
	Metric 18:	Sampling Adequacy	High	Nutritional/Metabolic: The number of animals used was adequate to evaluate the outcome of interest.; Nutritional/Metabolic: The study used adequate sampling
	Metric 19:	Blinding of Assessors	N/A	Nutritional/Metabolic: Blinding of assessors was not needed.; Nutritional/Metabolic: Blinding of samplers was not needed
	Metric 20:	Negative Control Response	Low	Nutritional/Metabolic: The body weight of the negative controls was not reported.; Nutritional/Metabolic: The biological response of the control group was not reported.
Domain 6: Confoundi	ng / Variable Cor	ntrol		
Domain o. Comound	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: Although the study did not report all information to determine confound
	Wietile 21.	and Procedures	Wicdiani	ing, reported information did not identify differences among study groups in confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss any differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Nutritional/Metabolic: Statistical methods were adequately reported.; Nutritional/Metabolic: Statistical analyses were adequately described.
	Metric 24:	Reporting of Data	Medium	All Outcomes: Changes to body weight were reported as body weight gain, which was calculated as total body weight difference between the means of terminal weight and the weight prior to the initiation of the study. Data were reported as a percent increase or decrease compared to control. The actual weights were not reported, and the error in the calculation was not reported.

## Overall Quality Determination

# High

**Study Citation:** 

Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM transgenic mice. Carcinogenesis 16(2):285-293.

Health

Missing 'other' target organ; Missing 'other' target organ;

Outcome(s):

Effect(s):

Reported Health

Missing 'other' target organ: Examination during gross necropsy: Gall bladder; Pancreas; Adrenal; Thyroid; Parathyroid; Pituitary, kidney, urinary bladder, ovary/testis, uterus/prostate, skin, mammary gland, lung, heart, skeletal muscle, bone (to include joint), bone marrow, brain (to include cerebral cortex, subcortical white matter, cerebellum and pons), cervical spinal cord, nerve (sciatic) and eveClinical biochemistry at time of termination: Alanine animotransferase; Urea nitrogen; Alkaline phosphatase; Creatinine; Aspartate aminotransferase; Calcium; Missing 'other' target organ: Examination during gross necropsy:Gall bladder; Pancreas; Adrenal; Thyroid; Parathyroid; Pituitary, kidney, urinary bladder, ovary/testis, uterus/prostate, skin, mammary gland, lung, heart, skeletal muscle, bone (to include joint), bone marrow, brain (to include cerebral cortex, subcortical white matter, cerebellum and pons), cervical spinal cord, nerve (sciatic) and eyeClinical biochemistry at time of termination: Alanine animotransferase; Urea nitrogen; Alkaline phosphatase;

Creatinine; Aspartate aminotransferase; Calcium;

**Duration:** Chemical: Chronic (>91 days) 40 weeks-Males

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

Domain	Metric		Rating	Comments	
Domain 1: Test Subst	ance				
	Metric 1:	Test Substance Identity	High	Missing 'other' target organ: The test compound was identified as 1,2-dichloroethane.; Missing 'other' target organ: The test compound was identified as 1,2-dichloroethane	
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was purchased from Fisher Scientific.	
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity was reported to be 99.8%	
Domain 2: Test Desig	n				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: An appropriate negative control (corn oil) was used.	
	Metric 5:	Positive Controls	N/A	Missing 'other' target organ: A positive control was not needed for this study.; Missing 'other' target organ: A positive control was not needed.	
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups.	
Domain 3: Exposure	Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Test substance dosing solutions were prepared weekly in corn oil and refrigerated until use; however, specific details on preparation procedures and storage (e.g., whether or not tightly capped to prevent volatilization) were not reported.	
	Metric 8:	Consistency of Exposure Administration	Medium	Missing 'other' target organ: Details of exposure administration are insufficiently reported. The total volume (mL) of corn oil per weight of the mouse was not reported. Gavage volumes for administration of the test substance is appropriate.; Missing 'other' target organ: The volume of corn oil used per kg of body weight was not reported. The gavage volumes used were appropriate for administration of the test substance.	
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses used were reported without ambiguity.	
	Metric 10:	Exposure Frequency and Duration	High	Missing 'other' target organ: The animals were administered the dose via gavage daily. Duration of exposure is adequate.; Missing 'other' target organ: The animals were administered the dose via gavage daily.	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: There were deficiencies regarding the number of exposure groups and dose spacing. The highest dose was lowered in weeks 1 to the lowest dose, resulting in both groups receiving the same dose level for the majority of the study.	
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route was acceptable for the administration of a volatile compound.	

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Study Citation:	Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM					
Health	transgenic mice. Carcinogenesis 16(2):285-293. Missing 'other' target organ; Missing 'other' target organ;					
Outcome(s):	wissing other target organ, wissing other target organ,					
Reported Health	Missing 'oth	er' target organ: Examination during gross necr	opsy:Gall bladder; P	ancreas; Adrenal; Thyroid; Parathyroid; Pituitary, kidney, urinary bladder,		
Effect(s):				, bone (to include joint), bone marrow, brain (to include cerebral cortex,		
				atic) and eyeClinical biochemistry at time of termination:Alanine animo-		
				transferase; Calcium; Missing 'other' target organ: Examination during		
				ry, kidney, urinary bladder, ovary/testis, uterus/prostate, skin, mammary		
				to include cerebral cortex, subcortical white matter, cerebellum and pons),		
			nistry at time of terr	nination:Alanine animotransferase; Urea nitrogen; Alkaline phosphatase;		
<b>.</b>		Aspartate aminotransferase; Calcium;				
Duration:		11 days) 40 weeks-Males				
Chemical:		bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	200612					
Domain		Metric	Rating	Comments		
Domain 4: Test Anima	als					
	Metric 13:	Test Animal Characteristics	Medium	Missing 'other' target organ: There were minor uncertainties in the reporting of test		
				animal characteristics (starting body weight), but these are unlikely to have a substant		
				impact on results.; Missing 'other' target organ: There were minor uncertainties in the reporting of test animal characteristics (starting body weight)but these are unlikely to		
				have a substantial impact on results.		
	Metric 14:	Adequacy and Consistency of Animal	Medium	All Outcomes: Most husbandry conditions were reported and were adequate and simil		
		Husbandry Conditions		for all groups. Humidity was not reported.		
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals was appropriate.		
Domain 5: Outcome A	Assessment					
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The choice of tissue to evaluate for changes to histopathology and the		
			8	serum biochemistry markers were appropriate to assess toxicities to multiple different		
				organs/systems.		
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: The duration of the study was reported to be 40 weeks, but the dose was		
	not administered for two weeks due to significant changes in body weight. It is not if the total time for the high dose group was 40 weeks with or without the break so					
				not clear if the outcomes were measured at the same time points.		
	Metric 18:	Sampling Adequacy	Medium	All Outcomes: Gross necropsy was only performed on mice that were had died or wer		
				terminated prior to the end of the study, and the exact numbers were not reported.		
	Metric 19:	Blinding of Assessors	N/A	Missing 'other' target organ: Blinding of assessors was not needed.; Missing 'other'		
	Metric 20:	Negative Control Response	Low	target organ: Blinding of assessors was not needed All Outcomes: The responses of the negative control were not reported.		
	Wictie 20.	regative control response	Low	An outcomes. The responses of the negative control were not reported.		
Domain 6: Confoundi	-		3.5 11			
	Metric 21:	Confounding Variables in Test Design	Medium	All Outcomes: Although the study did not report all information to determine confounding reported information did not identify differences among study groups in confound		
		and Procedures		ing, reported information did not identify differences among study groups in confound ing factors.		
	Metric 22:	Health Outcomes Unrelated to	Medium	All Outcomes: There was no information either to support or dismiss any differences		
		Exposure	1.10010111	among groups in animal attrition or health outcomes unrelated to exposure.		
			inued on next page	<del>-</del>		

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Study Citation: Health	Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM transgenic mice. Carcinogenesis 16(2):285-293.  Missing 'other' target organ; Missing 'other' target organ;					
Outcome(s):			·· ,			
Reported Health Effect(s):  Duration: Chemical: HERO ID:	Missing 'other' target organ: Examination during gross necropsy:Gall bladder; Pancreas; Adrenal; Thyroid; Parathyroid; Pituitary, kidney, urinary bladder, ovary/testis, uterus/prostate, skin, mammary gland, lung, heart, skeletal muscle, bone (to include joint), bone marrow, brain (to include cerebral cortex, subcortical white matter, cerebellum and pons), cervical spinal cord, nerve (sciatic) and eyeClinical biochemistry at time of termination:Alanine animotransferase; Urea nitrogen; Alkaline phosphatase; Creatinine; Aspartate aminotransferase; Calcium; Missing 'other' target organ: Examination during gross necropsy:Gall bladder; Pancreas; Adrenal; Thyroid; Parathyroid; Pituitary, kidney, urinary bladder, ovary/testis, uterus/prostate, skin, mammary gland, lung, heart, skeletal muscle, bone (to include joint), bone marrow, brain (to include cerebral cortex, subcortical white matter, cerebellum and pons), cervical spinal cord, nerve (sciatic) and eyeClinical biochemistry at time of termination:Alanine animotransferase; Urea nitrogen; Alkaline phosphatase; Creatinine; Aspartate aminotransferase; Calcium; Chronic (>91 days) 40 weeks-Males  1,1-Dichloroethane- Isomer: 1,2-Dichloroethane  200612					
Domain	Metric		Rating	Comments		
	Metric 23: Data Presentati	on and Analysis	High	Missing 'other' target organ: Statistical analyses were adequately described; Missing 'other' target organ: Statistical analyses were adequately described.		
	Metric 24: Reporting of D	ata	Uninformative	All Outcomes: Data from serum biochemistry and gross necropsy was not reported in the text or figures.		

# **Overall Quality Determination**

# Uninformative

HERO ID: 200612 Table: 6 of 6

Study Citation: Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM

transgenic mice. Carcinogenesis 16(2):285-293.

Health

Mortality; Mortality;

**Outcome(s):** 

**Reported Health** 

Mortality: Survival; Mortality: Survival;

Effect(s):

**Duration:** Chronic (>91 days) 40 weeks-Males

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	Mortality: The test compound was identified as 1,2-dichloroethane; Mortality: The test compound was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was purchased from Fisher Scientific.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity was reported to be 99.8%
Domain 2: Test Desig	gn			
·	Metric 4:	Negative and Vehicle Controls	High	Mortality: A corn oil control was used as a negative control.; Mortality: A corn oil negative control was used.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not needed.
	Metric 6:	Randomized Allocation of Animals	Low	Mortality: The study did not report how animals were allocated to study groups; Mortality: The study did not report how animals were allocated to study groups.
Domain 3: Exposure	Characterization			
•	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Test substance dosing solutions were prepared weekly in corn oil and refrigerated until use; however, specific details on preparation procedures and storage (e.g., whether or not tightly capped to prevent volatilization) were not reported.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: The volume of corn oil used per kg of body weight was not reported. The gavage volumes used were appropriate for administration of the test substance.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The animals were administered the dose via gavage daily.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: There were deficiencies regarding the number of exposure groups and dose spacing. The highest dose was lowered in weeks 1-3 to the lowest dose, resulting in both groups receiving the same dose level for the majority of the study.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route was acceptable for the administration of a volatile compound.
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: There were minor uncertainties in the reporting of test animal characteristics (starting body weight)but these are unlikely to have a substantial impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported and were adequate and similar for all groups. Humidity was not reported.
	Metric 15:	Number of Animals per Group	Medium	Mortality: The number of animals was suitable to determine mortality.; Mortality: The number of animals was appropriate to determine lethality.

#### Domain 5: Outcome Assessment

#### Continued on next page ...

# Human Health Hazard Animal Toxicology Evaluation

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Study Citation: Storer, R.D., Cartwright, M.E., Cook, W.O., Soper, K.A., Nichols, W.W. (1995). Short-term carcinogenesis bioassay of genotoxic procarcinogens in PIM transgenic mice. Carcinogenesis 16(2):285-293.

Health

Mortality; Mortality;

**Outcome(s):** 

**Reported Health** 

Mortality: Survival; Mortality: Survival;

**Effect(s):** 

**Duration:** Chronic (>91 days) 40 weeks-Males

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200612

Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Low	All Outcomes: The dose for the high dose group was changed multiple times throughout the beginning course of the study. It is not possible to assess to which dose or doses caused the lethality because the timing of the deaths was not reported.
	Metric 17:	Consistency of Outcome Assessment	High	Mortality: Lethality was assessed using the same protocol throughout the course of the study.; Mortality: Lethality was assessed consistently throughout the study
	Metric 18:	Sampling Adequacy	High	Mortality: Sampling was adequate to determine lethality.; Mortality: The sample number was appropriate to assess lethality.
	Metric 19:	Blinding of Assessors	N/A	Mortality: Blinding of assessors was not needed.; Mortality: Blinding of assessors was not needed for this study.
	Metric 20:	Negative Control Response	Medium	Mortality: There were deaths observed in the control group, but this could be attributed to the higher level of lymphoma observed in the PIM transgenic mice.; Mortality: There were deaths observed in the control group, but this could be attributes this to higher leve of lymphoma observed in transgenic PIM mice.
Jamain 6: Canfaun	ding / Variable Co	atral		
omani o. Comoun	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences among study groups in confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Mortality: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.; Mortality: There was no information either to support or dismiss any differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23: Metric 24:	Data Presentation and Analysis Reporting of Data	High High	All Outcomes: Statistical analyses were adequately described.  All Outcomes: Lethality was reported as the number of animals that survived to the time of sacrifice at 40 weeks. (n=27) The percentage of animals that survived was also reported.

## **Overall Quality Determination**

# High

Domain	Metric	Rating	Comments
HERO ID:	4451542		
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroetha	ane	
Duration:	large intestine, and gallbladder were evaluated Chronic (>91 days) 26 weeks	d for histopathology;	
Effect(s):	reported (Figure 1).; Skin/Connective Tissue	: Skin was evaluated for histopatholo	gical changes; Gastrointestinal: Esophagus, stomach, small intestine,
Reported Health	Cancer/Carcinogenesis: Incidence and multip	olicity of tumors was reported for tum	or types observed; Mortality: Survival during the exposure period was
Outcome(s):			
Health	dichloroethane in CB6F1-Tg rasH2 mice. To: Cancer/Carcinogenesis; Mortality; Skin/Conr		
<b>Study Citation:</b>	_		2017). Lung tumor induction by 26-week dermal application of 1,2-

Domain		Metric	Rating	Comments
Domain 1: Test Substance	e			
	Metric 1:	Test Substance Identity	High	All Outcomes: CAS No. 107-06-2 and lot No. PDJ0022 provided
	Metric 2:	Test Substance Source	High	All Outcomes: Chemical was purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan).
	Metric 3:	Test Substance Purity	High	Cancer/Carcinogenesis: The purity of the 1,2-DCE was 99.7%; Mortality: The purity of the 1,2-DCE was 99.7%.; Skin/Connective Tissue: The purity of the 1,2-DCE was 99.7%; Gastrointestinal: The purity of the 1,2-DCE was 99.7%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Cancer/Carcinogenesis: acetone (vehicle control), 80% ethanol (reference control); Mortality: acetone (vehicle control), 80% ethanol (reference control); Skin/Connective Tissue: Study type did not require but MNU, N-methyl-N-nitrosourea (positive control) was included; Gastrointestinal: acetone (vehicle control), 80% ethanol (reference control)
	Metric 5:	Positive Controls	N/A	All Outcomes: Study type did not require but MNU, N-methyl-N-nitrosourea (positive control) was included
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: rasH2 mice were divided by stratified randomization into 4 body weight–matched groups with 10 mice of each sex
Domain 3: Exposure Cha	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Deficiencies in reporting of test substance preparation and/or storage conditions are likely to have a substantial impact on results. The study does not sufficiently describe how the test substance was prepared (e.g., how frequently, and whether or not prepared fresh for each day of treatment, or stored)
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported and these may have a substantial impact on the results (e.g., it is unclear if the test substance remained on skin throughout the day; it is not mentioned whether the skin treatment site was covered, for example, to prevent ingestion due to licking)
	Metric 9:	Reporting of Doses/Concentrations	High	Cancer/Carcinogenesis: Administered doses/concentrations were reported without ambiguity.; Mortality: Administered doses/concentrations were reported without ambiguity; Skin/Connective Tissue: Administered doses/concentrations were reported without ambiguity; Gastrointestinal: Administered doses/concentrations were reported without ambiguity
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Exposure was only 3 days per week

		contin	ued from j	previous page				
Study Citation: Health	Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434. Cancer/Carcinogenesis; Mortality; Skin/Connective Tissue; Gastrointestinal;							
Outcome(s): Reported Health Effect(s):	reported (Fig		evaluated	reported for tumor types observed; Mortality: Survival during the exposure period was for histopathological changes; Gastrointestinal: Esophagus, stomach, small intestine,				
<b>Duration:</b>		1 days) 26 weeks	amology,					
Chemical: HERO ID:	1,1-Dichloro 4451542	bethane- Isomer: 1,2-Dichloroethane						
Domain		Metric	Rating	Comments				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Only one dose of 1,2-dichloroethane was tested; effects were observed (no NOAEL)				
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance.				
Domain 4: Test Animals	Matria 12.	Track Assistant Characteristics	TT: _1.					
	Metric 13:	Test Animal Characteristics	High	Cancer/Carcinogenesis: The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential of chemicals.; Mortality: The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential of chemicals.; Skin/Connective Tissue: The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential of chemicals.; Gastrointestinal: the test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential of chemicals.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: The mice were individually housed in transparent plastic cages on soft chip bedding in an animal room maintained under standard conditions (room temperature, 19.7 to 22.4 degrees C; relative humidity, 41% to 73%; ventilation, 10 or more air changes/hr, and a 12-hr light/dark cycle). Basal diet and Ichinomiya city tap water were available ad libitum throughout the experimental period. The animals were allowed a 9-day quarantine and acclimation period, during which body weights and health conditions were monitored. After confirmation of normal health status, they were entered into the experiment at the age of 7 weeks.				
	Metric 15:	Number of Animals per Group	Low	Cancer/Carcinogenesis: The test used only 10 animals/sex/group versus 50/sex/group for cancer bioassay.; Mortality: The test used only 10 animals/sex/group; Skin/Connective Tissue: The test used only 10 animals/sex/group; Gastrointestinal: The test used only 10 animals/sex/group				
Domain 5: Outcome A	assmart							
Domain 5: Outcome Asse	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology and the assessment methodology were sensitive and appropriate.				
		Contin	uied on ne	xt page				

		contin	ued from p	revious page			
Study Citation:  Health Outcome(s):	Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434. Cancer/Carcinogenesis; Mortality; Skin/Connective Tissue; Gastrointestinal;						
Reported Health	Cancer/Carc	inogenesis: Incidence and multiplicity of tr	imore was r	eported for tumor types observed; Mortality: Survival during the exposure period was			
Effect(s):				for histopathological changes; Gastrointestinal: Esophagus, stomach, small intestine,			
Effect(s).		ne, and gallbladder were evaluated for histor		tor instopathological changes, Gastromestinal. Esophagus, stomach, shair mestine,			
<b>Duration:</b>		1 days) 26 weeks	pathology,				
Chemical:		bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	4451542	,					
Domain		Metric	Rating	Comments			
	Metric 17:	Consistency of Outcome Assessment	High	Cancer/Carcinogenesis: he outcome assessment protocol were reported and outcomes were assessed consistently across study groups.; Mortality: The outcome assessment protocol were reported and outcomes were assessed consistently across study groups.; Skin/Connective Tissue: The outcome assessment protocol were reported and outcomes were assessed consistently across study groups.; Gastrointestinal: The outcome assessment protocol were reported and outcomes were assessed consistently across study groups.			
	Metric 18:	Sampling Adequacy	High	All Outcomes: Adequate sampling was used.			
	Metric 19:	Blinding of Assessors	N/A	Cancer/Carcinogenesis: Blinding is not applicable for study type.; Mortality: Blinding is not applicable for study type; Skin/Connective Tissue: Blinding is not applicable for study type; Gastrointestinal: Blinding is not applicable for study type			
	Metric 20:	Negative Control Response	High	Cancer/Carcinogenesis: The biological responses of the negative control groups were adequate. All 1, 2 Dichloroethane-treated rats developed hyperplastic and neoplastice lesions compared to acetone vehicle control. Incidence and multiplicity of adenoma and adenocarcinoma were often significantly different from acetone group at p < 0.01 and p<0.05.; Mortality: The biological responses of the negative control groups were adequate. Significant mortality observed in 1, 2-Dichloroethane-treated animals versus controls (Figure 1 A and B). Five female mice that had 1,2-DCE applied were euthanized in a moribund condition during weeks 17 to 25; these mice had bronchiolo-alveolar adenocarcinomas.; Skin/Connective Tissue: Histopathological outcomes for skin/subcutis were presented in Table 3.; Gastrointestinal: The biological responses of the negative control groups were adequate. Authors report that histopathology data in control groups were comparable to the published historical control data.			
Domain 6: Confoundin	g / Variable Co	ntrol					
Comounding	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	Cancer/Carcinogenesis: Appropriate statistical methods were applied.; Mortality: Statistical methods were appropriate. Survival curves were presented in Figure 1.; Skin/Connective Tissue: Histopathological outcomes for skin/subcutis were presented in Table 3.; Gastrointestinal: Appropriate statistical methods were applied.			
		Contin	nued on nex				

Study Citation: Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-

dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.

**Health Outcome(s):** 

Cancer/Carcinogenesis; Mortality; Skin/Connective Tissue; Gastrointestinal;

Reported Health Effect(s):

Cancer/Carcinogenesis: Incidence and multiplicity of tumors was reported for tumor types observed; Mortality: Survival during the exposure period was reported (Figure 1).; Skin/Connective Tissue: Skin was evaluated for histopathological changes; Gastrointestinal: Esophagus, stomach, small intestine,

large intestine, and gallbladder were evaluated for histopathology;

**Duration:** Chronic (>91 days) 26 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4451542

Domain		Metric	Rating	Comments
	Metric 24:	Reporting of Data	High	Cancer/Carcinogenesis: Incidence and multiplicity of bronchio-alveolar hyperplasia, adenoma and adenocarcinoma were reported.; Mortality: Survival data were presented in Figure 1 for treated and control male and female mice.; Skin/Connective Tissue: Histopathological outcomes for skin/subcutis were presented in Table 3.; Gastrointestinal: Gross pathological examinations for the tongue, salivary gland, esophagus, stomach, small intestine, large intestine were made at autopsy. Histopathological outcomes for the tongue, forestomach, duodenum, jejunum and ileum are in Table 3.

# Overall Quality Determination High

HERO ID: 4451542 Table: 2 of 5

**Study Citation:** Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434. Health Lung/Respiratory; Endocrine (Endocrine); Outcome(s): Reported Health Lung/Respiratory: Lung weights (mean and relative to body weight) were determined; nasal cavity, trachea, and lung were evaluated for histopathology; Effect(s): Endocrine (Endocrine): Pituitary, adrenal, and pancreas were evaluated for histopathology; Chronic (>91 days) 26 weeks **Duration:** Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 4451542 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Lung/Respiratory: CAS No. 107-06-2 and lot No. PDJ0022 were provided.; Endocrine (Endocrine): CAS No. 107-06-2 and lot No. PDJ0022 provided Metric 2: **Test Substance Source** High All Outcomes: Chemical was purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). Metric 3: Test Substance Purity High Lung/Respiratory: The purity of the 1,2-DCE was 99.7%.; Endocrine (Endocrine): The purity of the 1,2-DCE was 99.7% Domain 2: Test Design Metric 4: Negative and Vehicle Controls High All Outcomes: acetone (vehicle control), 80% ethanol (reference control) Metric 5: Positive Controls N/A All Outcomes: Study type did not require but MNU, N-methyl-N-nitrosourea (positive control) was included Metric 6: Randomized Allocation of Animals Medium Lung/Respiratory: rasH2 mice were divided by stratified randomization into 4body weight-matched groups with 10 mice of each sex.; Endocrine (Endocrine): rasH2 mice were divided by stratified randomization into 4 body weight-matched groups with 10 mice of each sex Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low Lung/Respiratory: Deficiencies in reporting of test substance preparation and/or storage conditions are likely to have a substantial impact on results. The study does not suffi-Substance ciently describe how the test substance was prepared (e.g., how frequently, and whether or not prepared fresh for each day of treatment, or stored).; Endocrine (Endocrine): Deficiencies in reporting of test substance preparation and/or storage conditions are likely to have a substantial impact on results. The study does not sufficiently describe how the test substance was prepared (e.g., how frequently, and whether or not prepared fresh for each day of treatment, or stored) Metric 8: Consistency of Exposure All Outcomes: Details of exposure administration are insufficiently reported and these Low may have a substantial impact on the results (e.g., it is unclear if the test substance re-Administration mained on skin throughout the day; it is not mentioned whether the skin treatment site was covered, for example, to prevent ingestion due to licking) Metric 9: Reporting of Doses/Concentrations High Lung/Respiratory: Administered doses/concentrations were reported without ambiguity; Endocrine (Endocrine): Administered doses/concentrations were reported without Metric 10: **Exposure Frequency and Duration** Medium Lung/Respiratory: Exposure was only 3 days per week; Endocrine (Endocrine): Exposure was only 3 days per week. Metric 11: Number of Exposure Groups and Low All Outcomes: Only one dose of 1,2-dichloroethane was tested; effects were observed Dose/Concentration Spacing (no NOAEL)

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	continued from previous page
<b>Study Citation:</b>	Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-
	dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.
Health	Lung/Respiratory; Endocrine (Endocrine);
Outcome(s):	
Reported Health	Lung/Respiratory: Lung weights (mean and relative to body weight) were determined; nasal cavity, trachea, and lung were evaluated for histopathology;
Effect(s):	Endocrine (Endocrine): Pituitary, adrenal, and pancreas were evaluated for histopathology;
<b>Duration:</b>	Chronic (>91 days) 26 weeks
Chaminal	11 Disklanders Inner 12 Disklanders

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Chemical: HERO ID:	1,1-Dichlore 4451542	bethane- Isomer: 1,2-Dichloroethane			
Domain		Metric	Rating	Comments	
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance.	
Domain 4: Test Animal	ls				
	Metric 13:	Test Animal Characteristics	High	Lung/Respiratory: The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential ofchemicals.; Endocrine (Endocrine): The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential of chemicals.	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions  Number of Animals per Group	High	Lung/Respiratory: The mice were individually housed in transparent plastic cageson soft chip bedding in an animal room maintained under standard conditions (room temperature, 19.7 to 22.4 degrees C; relative humidity, 41% to 73%; ventilation, 10 or more air changes/hr, and a 12-hr light/dark cycle). Basal diet and Ichinomiya city tap water were available ad libitum throughout the experimental period. The animals were allowed a 9-day quarantine and acclimation period, during which body weights and health conditions were monitored. After confirmation of normal health status, they were entered into the experiment at the age of 7 weeks.; Endocrine (Endocrine): The mice were individually housed in transparent plastic cages on soft chip bedding in an animal room maintained under standard conditions (room temperature, 19.7 to 22.4 degrees C; relative humidity, 41% to 73%; ventilation, 10 or more air changes/hr, and a 12-hr light/dark cycle). Basal diet and Ichinomiya city tap water were available ad libitum throughout the experimental period. The animals were allowed a 9-day quarantine and acclimation period, during which body weights and health conditions were monitored. After confirmation of normal health status, they were entered into the experiment at the age of 7 weeks. Lung/Respiratory: The test used only 10 animals/sex/group versus 50/sex/group for cancer bioassay; Endocrine (Endocrine): The test used only 10 animals/sex/group versus 50/sex/group for cancer bioassay;	
				Joseph Tol Cancer Bloassay.	
Domain 5: Outcome As					
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology and the assessment methodology were sensitive and appropriate.	
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The outcome assessment protocol were reported and outcomes were assessed consistently across study groups.	
	Metric 18:	Sampling Adequacy	High	Lung/Respiratory: Adequate sampling was used.; Endocrine (Endocrine): none	
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not applicable for study type.	

## Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

Study Citation: Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.

Health

Lung/Respiratory; Endocrine (Endocrine);

Outcome(s): Reported Health

Lung/Respiratory: Lung weights (mean and relative to body weight) were determined; nasal cavity, trachea, and lung were evaluated for histopathology;

**Effect(s):** Endocrine (Endocrine): Pituitary, adrenal, and pancreas were evaluated for histopathology;

**Duration:** Chronic (>91 days) 26 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4451542

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	High	Lung/Respiratory: The biological responses of the negative control groups were adequate. The absolute and relative lung weights in females treated with1,2-DCE were significantly increased compared to those of vehicle controls (Table 1), reflecting the macroscopic findings. There were no significant differences in lung weights between control and treated male animals.; Endocrine (Endocrine): The biological responses of the negative control groups were adequate.
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Lung/Respiratory: Appropriate statistical methods were applied. Statistical comparisons of body weight, food consumption,water intake, and organ weight were assessed using the F test. If homogeneous, the data were analyzed with Student's t test; ifheterogeneous, the data were analyzed with Aspin–Welch'stest. The significance of differences in gross pathology and histopathology of both neoplastic and nonneoplastic changeswas evaluated with the Fisher's exact probability test. TheWilcoxon test was employed for comparison of nonneoplasticlesions with degrees of severity. The p values less than 0.05were considered to be statistically significant.; Endocrine (Endocrine): Appropriate statistical methods were applied.
	Metric 24:	Reporting of Data	Low	Lung/Respiratory: Incidence of clinical signs (irregular respiration) during weeks 17-25) was not reported.; Endocrine (Endocrine): histopathological examinations were made for pituitary, adrenal and pancreas for control and treated animals. Authors did not report or present data for these outcomes.

# **Overall Quality Determination**

# High

Study Citation:	Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-
	dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.

Health **Outcome(s):**  Renal/Kidney; Hepatic/Liver; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Urinary (Urinary); Thyroid; Neurological/Behavioral; Immune/Hematological;

**Reported Health** Effect(s):

Renal/Kidney: Kidney weights (mean and relative to body weight) were determined; kidneys were evaluated for histopathology; Hepatic/Liver: Liver weights (mean and relative to body weight) were determined; liver was evaluated for histopathology; Ocular/Sensory: Eye, Harderian gland, tongue, and salivary gland were evaluated for histopathology; Reproductive/Developmental: Testis and ovary weights (mean and relative to body weight) were determined; prostate, seminal vesicle, epididymis, uterus, mammary gland, and vagina were evaluated for histopathology; Cardiovascular: Heart weights (mean and relative to body weight) were determined; circulatory system and aorta were evaluated for histopathology; Urinary (Urinary): Urinary bladder was evaluated for histopathology; Thyroid: Thyroid and parathyroid were evaluated for histopathology; Neurological/Behavioral: Clinical signs during the exposure period were evaluated; brain weights (mean and relative to body weight) were determined; spinal cord and sciatic nerve were evaluated for histopathology; Immune/Hematological: Thymus and spleen weights (mean and relative to body weight) were determined; lymph nodes (mandibular, mesenteric), thymus, and bone and bone marrow were evaluated for histopathology;

**Duration:** 

Chronic (>91 days) 26 weeks

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric	1: Test Substance Identity	High	All Outcomes: CAS No. 107-06-2 and lot No. PDJ0022 provided
Metric	2: Test Substance Source	High	All Outcomes: Chemical was purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan).
Metric	3: Test Substance Purity	High	All Outcomes: The purity of the 1,2-DCE was 99.7%
Domain 2: Test Design			
Metric	4: Negative and Vehicle Controls	High	All Outcomes: acetone (vehicle control), 80% ethanol (reference control)
Metric	5: Positive Controls	N/A	All Outcomes: Study type did not require but MNU, N-methyl-N-nitrosourea (positive control) was included
Metric	6: Randomized Allocation of Animals	Medium	All Outcomes: rasH2 mice were divided by stratified randomization into 4 body weight-matched groups with 10 mice of each sex
Domain 3: Exposure Characteriza	ation		
Metric		Low	All Outcomes: Deficiencies in reporting of test substance preparation and/or storage conditions are likely to have a substantial impact on results. The study does not sufficiently describe how the test substance was prepared (e.g., how frequently, and whether or not prepared fresh for each day of treatment, or stored)
Metric	8: Consistency of Exposure Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported and these may have a substantial impact on the results (e.g., it is unclear if the test substance remained on skin throughout the day; it is not mentioned whether the skin treatment site was covered, for example, to prevent ingestion due to licking)

	Francisco Lange
Study Citation:	Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.
Health	Renal/Kidney; Hepatic/Liver; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Urinary (Urinary); Thyroid; Neurological/Behavioral; Im-
Outcome(s):	mune/Hematological;
Reported Health	Renal/Kidney: Kidney weights (mean and relative to body weight) were determined; kidneys were evaluated for histopathology; Hepatic/Liver: Liver
Effect(s):	weights (mean and relative to body weight) were determined; liver was evaluated for histopathology; Ocular/Sensory: Eye, Harderian gland, tongue, and salivary gland were evaluated for histopathology; Reproductive/Developmental: Testis and ovary weights (mean and relative to body weight) were determined; prostate, seminal vesicle, epididymis, uterus, mammary gland, and vagina were evaluated for histopathology; Cardiovascular: Heart weights (mean and relative to body weight) were determined; circulatory system and aorta were evaluated for histopathology; Urinary (Urinary): Urinary bladder was evaluated for histopathology; Thyroid: Thyroid and parathyroid were evaluated for histopathology; Neurological/Behavioral: Clinical signs during the exposure period were evaluated; brain weights (mean and relative to body weight) were determined; spinal cord and sciatic nerve were evaluated for histopathology; Immune/Hematological: Thymus and spleen weights (mean and relative to body weight) were determined; lymph nodes (mandibular, mesenteric), thymus, and bone and bone marrow were evaluated for histopathology;
Duration:	Chronic (>91 days) 26 weeks
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4451542
D	Matrix Dating Comments

Domain		Metric	Rating	Comments
	Metric 9:	Reporting of Doses/Concentrations	High	Renal/Kidney: Administered doses/concentrations were reported without ambiguity.; Hepatic/Liver: Administered doses/concentrations were reported without ambiguity; Ocular/Sensory: Administered doses/concentrations were reported without ambiguity; Reproductive/Developmental: Administered doses/concentrations were reported without ambiguity; Cardiovascular: Administered doses/concentrations were reported without ambiguity; Urinary (Urinary): Administered doses/concentrations were reported without ambiguity; Thyroid: Administered doses/concentrations were reported without ambiguity; Neurological/Behavioral: Administered doses/concentrations were reported without ambiguity; Immune/Hematological: Administered doses/concentrations were reported without ambiguity
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Exposure was only 3 days per week
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Only one dose of 1,2-dichloroethane was tested; effects were observed (no NOAEL)
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential of chemicals.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: The mice were individually housed in transparent plastic cages on soft chip bedding in an animal room maintained under standard conditions (room temperature, 19.7 to 22.4 degrees C; relative humidity, 41% to 73%; ventilation, 10 or more air changes/hr, and a 12-hr light/dark cycle). Basal diet and Ichinomiya city tap water were available ad libitum throughout the experimental period. The animals were allowed a 9-day quarantine and acclimation period, during which body weights and health conditions were monitored. After confirmation of normal health status, they were entered into the experiment at the age of 7 weeks.
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Metric 17:

Metric 18:

Metric 19:

Consistency of Outcome Assessment

Sampling Adequacy

Blinding of Assessors

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		continued from p	previous page					
Study Citation:	Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.  Renal/Kidney; Hepatic/Liver; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Urinary (Urinary); Thyroid; Neurological/Behavioral; Im-							
Health Outcome(s):		; Reproductive/Deve	elopmental; Cardiovascular; Orinary (Orinary); Inyrold; Neurological/Benavioral; Im-					
Reported Health Effect(s):  Duration: Chemical: HERO ID:	mune/Hematological; Renal/Kidney: Kidney weights (mean and relative to body weight) were determined; kidneys were evaluated for histopathology; Hepatic/Liver: Live weights (mean and relative to body weight) were determined; liver was evaluated for histopathology; Ocular/Sensory: Eye, Harderian gland, tongue and salivary gland were evaluated for histopathology; Reproductive/Developmental: Testis and ovary weights (mean and relative to body weight) were determined; prostate, seminal vesicle, epididymis, uterus, mammary gland, and vagina were evaluated for histopathology; Cardiovascular: Heart weigh (mean and relative to body weight) were determined; circulatory system and aorta were evaluated for histopathology; Urinary (Urinary): Urinary bladd was evaluated for histopathology; Thyroid: Thyroid and parathyroid were evaluated for histopathology; Neurological/Behavioral: Clinical signs during the exposure period were evaluated; brain weights (mean and relative to body weight) were determined; spinal cord and sciatic nerve were evaluated for histopathology; Immune/Hematological: Thymus and spleen weights (mean and relative to body weight) were determined; lymph nodes (mandibulative), thymus, and bone and bone marrow were evaluated for histopathology;  Chronic (>91 days) 26 weeks  1,1-Dichloroethane- Isomer: 1,2-Dichloroethane  4451542							
Domain Domain	Metric	Rating	Comments					
Domain	Metric 15: Number of Animals per Group	Low	Renal/Kidney: The test used only 10 animals/sex/group versus 50/sex/group for cancer bioassay.; Hepatic/Liver: The test used only 10 animals/sex/group; Ocular/Sensory: The test used only 10 animals/sex/group; Reproductive/Developmental: The test used only 10 animals/sex/group; Cardiovascular: The test used only 10 animals/sex/group versus 50/sex/group for cancer bioassay; Urinary (Urinary): The test used only 10 animals/sex/group versus 50/sex/group for cancer bioassay; Thyroid: The test used only 10 animals/sex/group; Neurological/Behavioral: The test used only 10 animals/sex/group versus 50/sex/group for cancer bioassay; Immune/Hematological: The test used only 10 animals/sex/group versus 50/sex/group for cancer bioassay					
Domain 5: Outcome A	Assessment Metric 16: Outcome Assessment Methodo	logy High	All Outcomes: The outcome assessment methodology and the assessment methodology					
			were sensitive and appropriate.					

#### Continued on next page ...

High

High

N/A

All Outcomes: The outcome assessment protocol were reported and outcomes were

Renal/Kidney: Blinding is not applicable for study type.; Hepatic/Liver: Blinding is not

applicable for study type; Ocular/Sensory: Blinding is not applicable for study type.; Reproductive/Developmental: Blinding is not applicable for study type.; Cardiovascular: Blinding is not applicable for study type; Urinary (Urinary): Blinding is not applicable for study type; Thyroid: Blinding is not applicable for study type; Neurological/Behavioral: Blinding is not applicable for study type; Immune/Hematological:

assessed consistently across study groups.

Blinding is not applicable for study type

All Outcomes: Adequate sampling was used.

## Human Health Hazard Animal Toxicology Evaluation

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**Study Citation:** 

Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.

Health

Renal/Kidney; Hepatic/Liver; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Urinary (Urinary); Thyroid; Neurological/Behavioral; Immune/Hematological;

Outcome(s): Reported Health Effect(s):

Renal/Kidney: Kidney weights (mean and relative to body weight) were determined; kidneys were evaluated for histopathology; Hepatic/Liver: Liver weights (mean and relative to body weight) were determined; liver was evaluated for histopathology; Ocular/Sensory: Eye, Harderian gland, tongue, and salivary gland were evaluated for histopathology; Reproductive/Developmental: Testis and ovary weights (mean and relative to body weight) were determined; prostate, seminal vesicle, epididymis, uterus, mammary gland, and vagina were evaluated for histopathology; Cardiovascular: Heart weights (mean and relative to body weight) were determined; circulatory system and aorta were evaluated for histopathology; Urinary (Urinary): Urinary bladder was evaluated for histopathology; Thyroid: Thyroid and parathyroid were evaluated for histopathology; Neurological/Behavioral: Clinical signs during the exposure period were evaluated; brain weights (mean and relative to body weight) were determined; spinal cord and sciatic nerve were evaluated for histopathology; Immune/Hematological: Thymus and spleen weights (mean and relative to body weight) were determined; lymph nodes (mandibular, mesenteric), thymus, and bone and bone marrow were evaluated for histopathology;

**Duration:** 

Chronic (>91 days) 26 weeks

Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		3.6.4.1		
		Metric	Rating	Comments
	Metric 20:	Negative Control Response	High	Renal/Kidney: In the kidney, distal tubular mild karyomegaly was increased in 1,2-DCE-treated rasH2 mice of both sexes. In females, the karyomegaly was accompanied by tubular degeneration. These findings might be associated with the slight increase of relative kidney weights in the female group (data not shown).; Hepatic/Liver: No differences in liver histopathology/sarcoma between treated and control animals (no sarcomas were observed).; Ocular/Sensory: The biological responses of the negative control groups were adequate. There were no ocular histopathological changes in controls versus treated animals.; Reproductive/Developmental: There were no histopathological changes in reproductive organs for treated versus control animals (e.g. adenocarcinoma, adenoma, polyps) as indicated in Table 3.; Cardiovascular: There were no histopathological changes in cardiovascular/circulatory system for treated versus control male animals (e.g. hemangioma, hemangiosarcoma) as indicated in Table 3. One acetone-treated female mouse developed a hemangiosarcoma.; Urinary (Urinary): The biological responses of the negative control groups were adequate. No histopathological changes in the urethra were reported, except for 1 acetone-treated female mouse.; Thyroid: The biological responses of the negative control groups were adequate. No histopathological changes were noted between treated versus control animals.; Neurological/Behavioral: The biological responses of the negative control groups were adequate. No histopathological: The biological responses of the negative control groups were adequate. No histopathological: The biological responses of the negative control groups were adequate. No histopathological changes were noted between treated versus control animals.
Domain 6: Confounding	g / Variable Cor	itrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.

**Study Citation:** Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434. Health Renal/Kidney; Hepatic/Liver; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Urinary (Urinary); Thyroid; Neurological/Behavioral; Im-**Outcome(s):** mune/Hematological; **Reported Health** Renal/Kidney: Kidney weights (mean and relative to body weight) were determined; kidneys were evaluated for histopathology; Hepatic/Liver: Liver Effect(s): weights (mean and relative to body weight) were determined; liver was evaluated for histopathology; Ocular/Sensory: Eye, Harderian gland, tongue, and salivary gland were evaluated for histopathology; Reproductive/Developmental: Testis and ovary weights (mean and relative to body weight) were determined; prostate, seminal vesicle, epididymis, uterus, mammary gland, and vagina were evaluated for histopathology; Cardiovascular: Heart weights

(mean and relative to body weight) were determined; circulatory system and aorta were evaluated for histopathology; Urinary (Urinary): Urinary bladder was evaluated for histopathology; Thyroid: Thyroid and parathyroid were evaluated for histopathology; Neurological/Behavioral: Clinical signs during the exposure period were evaluated; brain weights (mean and relative to body weight) were determined; spinal cord and sciatic nerve were evaluated for histopathology; Immune/Hematological: Thymus and spleen weights (mean and relative to body weight) were determined; lymph nodes (mandibular, mesenteric), thymus, and bone and bone marrow were evaluated for histopathology:

**Duration: Chemical:**  Chronic (>91 days) 26 weeks

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	High	Renal/Kidney: Appropriate statistical methods were applied. Statistical comparisons of organ weight were assessed using the F test. If homogeneous, the data were analyzed with Student's t test; ifheterogeneous, the data were analyzed with Aspin–Welch'stest.; Hepatic/Liver: Appropriate statistical methods were applied. Statistical comparisons of organ weight were assessed using the F test. If homogeneous, the data were analyzed with Student's t test; if heterogeneous, the data were analyzed with Aspin–Welch's test.; Ocular/Sensory: Appropriate statistical methods were applied.; Reproductive/Developmental: Statistical methods were appropriate.; Cardiovascular: Appropriate statistical methods were applied.; Thyroid: Appropriate statistical methods were applied.; Neurological/Behavioral: Appropriate statistical methods were applied.; Immune/Hematological: Appropriate statistical methods were applied.
	Metric 24:	Reporting of Data	Medium	Renal/Kidney: Increases of relative kidney weights in the female mice were not shown. Hepatic/Liver: Relative liver weights were not presented.; Ocular/Sensory: Gross pathological examinations for the eye were made at autopsy. Relative weights were not presented. Histopathological outcomes for the retina were reported in Table 3.; Reproductive/Developmental: Organ weights were recorded but relative weights not presented. Gross pathological examinations for reproductive organs (prostate, seminal vesicle, epididymis, uterus, mammary gland, vagina) were made at autopsy. Histopathological outcomes for the uterus were reported in Table 3. It is assumed that no changes were observed in males as none were reported.; Cardiovascular: Organ weights were recorded but relative weights for the heart was not presented. Gross pathological examinations for the circulatory system were made at autopsy. Histopathological outcomes were reported in Table 3.; Urinary (Urinary): Gross pathological examinations for the urinary bladder and urethra were made at autopsy. Histopathological outcomes for the urethra were reported in Table 3. Relative weights not presented.; Thyroid: Gross pathological examinations for the thyroid, parathyroid were made at autopsy. Relative weights not presented.; Neurological/Behavioral: Gross pathological examinations for the brain and spinal cord were made at autopsy. Relative weights not presented.; Immune/Hematological: Gross pathological examinations for the spleen, bone marrow, thymus were made at autopsy. Relative weights not presented.

Study Citation: Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-

dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.

Health Renal/Kidney; Hepatic/Liver; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Urinary (Urinary); Thyroid; Neurological/Behavioral; Immune/Hematological;

utcome(s): mune/Hematological;

**Reported Health**Renal/Kidney: Kidney weights (mean and relative to body weight) were determined; kidneys were evaluated for histopathology; Hepatic/Liver: Liver weights (mean and relative to body weight) were determined; liver was evaluated for histopathology; Ocular/Sensory: Eye, Harderian gland, tongue,

weights (mean and relative to body weight) were determined; niver was evaluated for histopathology; Certiar/sensory: Eye, Harderian gland, tongue, and salivary gland were evaluated for histopathology; Reproductive/Developmental: Testis and ovary weights (mean and relative to body weight) were determined; prostate, seminal vesicle, epididymis, uterus, mammary gland, and vagina were evaluated for histopathology; Cardiovascular: Heart weights (mean and relative to body weight) were determined; circulatory system and aorta were evaluated for histopathology; Urinary (Urinary): Urinary bladder was evaluated for histopathology; Thyroid: Thyroid and parathyroid were evaluated for histopathology; Neurological/Behavioral: Clinical signs during the exposure period were evaluated; brain weights (mean and relative to body weight) were determined; spinal cord and sciatic nerve were evaluated for histopathology; Immune/Hematological: Thymus and spleen weights (mean and relative to body weight) were determined; lymph nodes (mandibular,

mesenteric), thymus, and bone and bone marrow were evaluated for histopathology;

**Duration:** Chronic (>91 days) 26 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric	Rating	Comments	
Overall Quality Dete	ermination	High		

Study Citation: Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.

Health Musculoskeletal

**Outcome(s):** 

**Reported Health** 

Skeletal muscle was evaluated for histopathology

**Effect(s):** 

**Duration:** Chronic (>91 days) 26 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	CAS No. 107-06-2 and lot No. PDJ0022 provided
	Metric 2:	Test Substance Source	High	Chemical was purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan).
	Metric 3:	Test Substance Purity	High	The purity of the 1,2-DCE was 99.7%
Domain 2: Test Design				
Č	Metric 4:	Negative and Vehicle Controls	High	acetone (vehicle control), 80% ethanol (reference control)
	Metric 5:	Positive Controls	N/A	Study type did not require but MNU, N-methyl-N-nitrosourea (positive control) was included
	Metric 6:	Randomized Allocation of Animals	Medium	rasH2 mice were divided by stratified randomization into 4 body weight-matched groups with 10 mice of each sex
Damain 2. Evmanum Ch				
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Low	Deficiencies in reporting of test substance preparation and/or storage conditions are likely to have a substantial impact on results. The study does not sufficiently describe how the test substance was prepared (e.g., how frequently, and whether or not prepared fresh for each day of treatment, or stored)
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and these may have a substantial impact on the results (e.g., it is unclear if the test substance remained on skin throughout the day; it is not mentioned whether the skin treatment site was covered, for example, to prevent ingestion due to licking)
	Metric 9:	Reporting of Doses/Concentrations	High	Administered doses/concentrations were reported without ambiguity
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure was only 3 days per week
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose of 1,2-dichloroethane was tested; effects were observed (no NOAEL)
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.
Domain 4: Test Animals	s.			
Domain 7. Test Allillidi	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential of chemicals.

<b>Study Citation:</b>	Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-
	dichloroethane in CR6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434

Health

Musculoskeletal

Outcome(s): Reported Health

Skeletal muscle was evaluated for histopathology

**Effect(s):** 

**Duration:** Chronic (>91 days) 26 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The mice were individually housed in transparent plastic cages on soft chip bedding in an animal room maintained under standard conditions (room temperature, 19.7 to 22.4 degrees C; relative humidity, 41% to 73%; ventilation, 10 or more air changes/hr, and a 12-hr light/dark cycle). Basal diet and Ichinomiya city tap water were available ad libitum throughout the experimental period. The animals were allowed a 9-day quarantine and acclimation period, during which body weights and health conditions were monitored. After confirmation of normal health status, they were entered into the experiment at the age of 7 weeks.
	Metric 15:	Number of Animals per Group	Low	The test used only 10 animals/sex/group versus 50 animals/sex/group for cancer bioassays
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 17:	Consistency of Outcome Assessment	High	The outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Adequate sampling was used.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not applicable for study type
	Metric 20:	Negative Control Response	Low	Histopathological outcomes for musculature were reported in Table 3. Myopathy were observed at almost similar levels in both male and female control and treated animals. However these findings were not explained.
Domain 6: Confound	ing / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Appropriate statistical methods were applied.
	Metric 24:	Reporting of Data	Medium	Organ weights were recorded but relative weights not presented. Gross pathological examinations for skeletal muscle, bone and bone marrow) were made at autopsy. Histopathological outcomes for musculature were reported in Table 3. Myopathy were observed in the both male and female control and treated animals. However these findings were not explained.

**Study Citation:** Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434. Health Nutritional/Metabolic

**Outcome(s):** 

Effect(s):

**Reported Health** 

Individual body weights were recorded weekly for the first 14 weeks and every other week thereafter during the experimental period. Body weight changes over the 26-week treatment period were reported (Figure 2). Food consumption and water intake were measured over a 2-day period before each weighing.

HERO ID: 4451542 Table: 5 of 5

**Duration:** Chronic (>91 days) 26 weeks

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

Domain		Metric	Rating	Comments
Domain 1: Test Substan	ice			
	Metric 1:	Test Substance Identity	High	CAS No. 107-06-2 and lot No. PDJ0022 provided
	Metric 2:	Test Substance Source	High	Chemical was purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan).
	Metric 3:	Test Substance Purity	High	The purity of the 1,2-DCE was 99.7%.
Domain 2: Test Design				
C	Metric 4:	Negative and Vehicle Controls	High	acetone (vehicle control), 80% ethanol (reference control)
	Metric 5:	Positive Controls	N/A	Study type did not require but MNU, N-methyl-N-nitrosourea (positive control) was included
	Metric 6:	Randomized Allocation of Animals	Medium	asH2 mice were divided by stratified randomization into 4 body weight-matched groups with 10 mice of each sex
Domain 2: Evnagura Ch	naraatarization			
Domain 3: Exposure Ch	Metric 7:	Preparation and Storage of Test Substance	Low	Deficiencies in reporting of test substance preparation and/or storage conditions are likely to have a substantial impact on results. The study does not sufficiently describe how the test substance was prepared (e.g., how frequently, and whether or not prepared fresh for each day of treatment, or stored)
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported and these may have a substantial impact on the results (e.g., it is unclear if the test substance remained on skin throughout the day; it is not mentioned whether the skin treatment site was covered, for example, to prevent ingestion due to licking)
	Metric 9:	Reporting of Doses/Concentrations	High	Administered doses/concentrations were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure was only 3 days per week
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose of 1,2-dichloroethane was tested; effects were observed (no NOAEL)
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.
Domain 4: Test Animal	S			
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the carcinogenic potential of chemicals.

Human Health Hazard Animal Toxicology Evaluation HERO ID: 4451542 Table: 5 of 5

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**Study Citation:** Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.

Health

Effect(s):

Nutritional/Metabolic

**Outcome(s): Reported Health** 

Individual body weights were recorded weekly for the first 14 weeks and every other week thereafter during the experimental period. Body weight changes over the 26-week treatment period were reported (Figure 2). Food consumption and water intake were measured over a 2-day period before each weighing.

**Duration:** Chronic (>91 days) 26 weeks

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 4451542

HERU ID:	4431342			
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The mice were individually housed in transparent plastic cages on soft chip bedding in an animal room maintained under standard conditions (room temperature, 19.7 to 22.4 degrees C; relative humidity, 41% to 73%; ventilation, 10 or more air changes/hr, and a 12-hr light/dark cycle). Basal diet and Ichinomiya city tap water were available ad libitum throughout the experimental period. The animals were allowed a 9-day quarantine and acclimation period, during which body weights and health conditions were monitored. After confirmation of normal health status, they were entered into the experiment at the age of 7 weeks.
	Metric 15:	Number of Animals per Group	Low	The test used only 10 animals/sex/group
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology and the assessment methodology were sensitive and appropriate.
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment of body weight across groups) were limited.
	Metric 18:	Sampling Adequacy	High	Adequate sampling was used.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not applicable for study type.
	Metric 20:	Negative Control Response	High	The biological responses of the negative control groups were adequate. Significantly decreased body weight changes at $p<0.01$ and $p<0.05$ were found in females treated with 1,2-DCE from week 18 to the end of the experiment but not in males, compared to Acetone controls.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Appropriate statistical methods were applied. Statistical comparisons of body weight, food consumption, water intake, and organ weight were assessed using the F test. If homogeneous, the data were analyzed with Student's t test; if heterogeneous, the data were analyzed with Aspin–Welch's test.
	Metric 24:	Reporting of Data	Low	Measures of variability with number per group was not provided for body weight changes (shown in Figure 2). Incidence of clinical signs (emaciation during weeks 17-25) was not reported.

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1,1-Dichloroethane

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Study Citation: Suguro, M., Numano, T., Kawabe, M., Doi, Y., Imai, N., Mera, Y., Tamano, S. (2017). Lung tumor induction by 26-week dermal application of 1,2-

dichloroethane in CB6F1-Tg rasH2 mice. Toxicologic Pathology 45(3):427-434.

**Health** Nutritional/Metabolic

**Outcome(s):** 

Effect(s):

Reported Health

Individual body weights were recorded weekly for the first 14 weeks and every other week thereafter during the experimental period. Body weight changes over the 26-week treatment period were reported (Figure 2). Food consumption and water intake were measured over a 2-day period before each weighing.

HERO ID: 4451542 Table: 5 of 5

**Duration:** Chronic (>91 days) 26 weeks

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 4451542

Domain Metric Rating Comments

Overall Quality Determination High

HERO ID: 194588 Table: 1 of 3

1,1-Dichloroethane

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

**Health** Mortality

**Outcome(s):** 

Reported Health

Effect(s):

effort(s).

survival

**Duration:** Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment during gestation, lactation-through weaning. Then females were returned to communal cages to repeat the treatment regimen for 5 pregnancies over 2 years

Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
Domain 1: Test Subst	ance			
	Metric 1:	Test Substance Identity	High	The test chemical was reported by name as ethylene dichloride (1,2 dichloroethane). CASRN was not reported.
	Metric 2:	Test Substance Source	High	The test substance source was not reported; however, it was analytically verified by the laboratory.
	Metric 3:	Test Substance Purity	Low	Purity of test substance was not reported.
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	High	The study included concurrent negative controls (implied unfumigated diet) and conditions were not explicitly stated, but assumed to be consistent with the treated animals.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	There were no reported details on allocation or distribution of animals.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	The test substance preparation was as follows: feed was exposed to the test substance in hermetically sealed containers and stored in polyvinyl bags coated in polyamide or sealed hermetically in glass jars with a polyamide layered plastic lid. The fumigated feed was stored for a maximum storage duration of 10 days during which loss was analyzed to be approximately 5%.
	Metric 8:	Consistency of Exposure Administration	Medium	The test substance was administered via furnigated diet. Feed mash was administered for a limited period (1 or 2 hours) twice a day at the same time each day. Consumption and concentration of the test substance was measured in effort to maintain consistency. It was not reported whether animals were trained to the limited feeding schedule prior to implementation.
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**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health

Mortality

**Outcome(s):** 

Reported Health

Effect(s):

survival

**Duration:** 

Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment during gestation, lactation-through weaning. Then females were returned to communal cages to repeat the treatment regimen for 5 pregnancies over 2 years

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 194588

HERO ID:

HERO ID:	194588			
Domain		Metric	Rating	Comments
Domain	Metric 9:	Reporting of Doses/Concentrations	Medium	Administered diet concentration (ppm) were reported. Diet was weighed (weekly) in order to determine amount consumed but those results were not reported. Feed was consumed primarily in the evening time frame with the majority during the first hour indicating the dose was consumed largely in a small time frame. Doses present in the diet after the 1-2h consumption period were reportedly 60-70% that of initially in masl and the authors stated, "since the amount eaten and the residue level were known, the amount of fumigant actually consumed was calculated with fair accuracy", therefore, it is implied that this was accounted for. It is unclear if the introduction of diet for limited time frames caused any initial changes in food consumption, thus altering the dose consumed, though the authors reported the animals "grew accustomed to consuming it quickly". It is unclear if the amount consumed is consistent to that consumed if feed were presented ad libitum. The doses could potentially be calculated.
	Metric 10:	Exposure Frequency and Duration	Uninformative	Exposure frequency was 1-2 hours, twice daily, for 7 days/week differed from typical study design but was altered due to test substance volatility. Exposure duration appears to be intermittent: reported exposure was for 6 weeks during premating, it was stated that during mating, animals were on a control diet, and following mating (gestation-weaning) it was unclear if the treated diet was continued. After weaning, females were added to communal cages and it was implied that the intermittent exposure was repeate (for 4-5 pregnancies total).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The number of exposure groups was limited to 2 treated groups and a control. Dose spacing did not encompass any effects therefore it is unclear whether spacing was appropriate.
	Metric 12:	Exposure Route and Method	Medium	The exposure method was not suited to the test substance. The test substance is volatile and it was prepared in the diet. However, the authors attempted to mitigate the issues o volatility in feed via sealed fumigation, limited feeding times and monitoring of the test substance residues.
Domain 4: Test Anim	nals			
	Metric 13:	Test Animal Characteristics	Low	Animal characteristics were not completely reported. The details included the species (rats) and sex (female). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not sufficiently reported to evaluate adequacy.
	Metric 15:	Number of Animals per Group	Low	The number of animals (18/group) were reported and were adequate for this study type

Domain 5: Outcome Assessment

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Study Citation:		Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111.				
Health	Mortality					
Outcome(s):	-					
Reported Health	survival					
Effect(s):						
<b>Duration:</b>	Reproductive	e/Developmental Females, intermittent exposi	ure: treated during 6 week	ks premating, not treated during 10 d mating period, Unclear treatment		
			were returned to commu	anal cages to repeat the treatment regimen for 5 pregnancies over 2 years		
Chemical:		bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	194588					
Domain		Metric	Rating	Comments		
	Metric 16:	Outcome Assessment Methodology	High	Animals were observed for morbidity and mortality. The outcome assessment was sensi tive and appropriate for the outcome of interest.		
	Metric 17:	Consistency of Outcome Assessment	High	The outcome assessment was briefly described, previously cited and was carried out consistently across groups.		
	Metric 18:	Sampling Adequacy	High	All animals were sampled for the outcome of interest as reported in month 0 of table 5.		
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary because this outcome of interest is not subjective in nature or is not required for this outcome of interest.		
	Metric 20:	Negative Control Response	Low	Negative control animals had reduced survival.		
Domain 6: Confound		ntrol				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Information to determine confounding was not reported. No differences were identified from the reported information. With the measured residue of the test substance being 60-70% in feed after the feeding period (of 1-2 hours) it is possible that due to the volatility of the test substance, some was inhaled. Information regarding food consumption was insufficient so it is unclear whether the animals consumed an amount similar to that of feed presented ad libitum. It is unclear whether there were palatability issues (if there were, they may have been complicated by the intermittent feeding).		
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	It was reported that animals at 14 months and greater exhibited chronic respiratory disease- confirmed by necropsy that reduced survival. Additionally, reproduction ceased as animals aged.		
	Metric 23:	Data Presentation and Analysis	Low	Statistical methods were used and reported as analysis of variance with Duncan multiple range test pairwise comparison. Significance was denoted in tables and figures. It is unclear whether this method was applied to survival, but is not an appropriate test for survival.		
	Metric 24:	Reporting of Data	Medium	The study data were reported in a table for each group and discussed in the text.		
Overall Qua	lity Detern	nination	Uninformative			

HERO ID: 194588 Table: 2 of 3

Study Citation:	Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111.					
Health		ey; Hepatic/Liver;				
Outcome(s):						
Reported Health	Renal/Kidney: serum urea, uric acid, glucose; Hepatic/Liver: liver fat content, serum total protein, cholesterol, ALT, AST;					
Effect(s):	Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment					
<b>Duration:</b>						
			s were returned to com	munal cages to repeat the treatment regimen for 5 pregnancies over 2 years		
Chemical:	1,1-Dichlor	oethane- Isomer: 1,2-Dichloroethane				
HERO ID:	194588					
Domain		Metric	Rating	Comments		
Domain 1: Test Substan	ce					
	Metric 1:	Test Substance Identity	High	All Outcomes: The test chemical was reported by name as ethylene dichloride (1,2 dichloroethane). CASRN was not reported.		
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source was not reported; however, it was analytically verified by the laboratory.		
	Metric 3:	Test Substance Purity	Low	All Outcomes: Purity of test substance was not reported.		
Domain 2: Test Design						
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The study included concurrent negative controls (implied unfumigated diet) and conditions were not explicitly stated, but assumed to be consistent with the treated animals.		
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.		
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: There were no reported details on allocation or distribution of animals.		
Domain 3: Exposure Ch	paracterization					
Domain 3. Exposure Cr.	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The test substance preparation was as follows: feed was exposed to the test substance in hermetically sealed containers and stored in polyvinyl bags coated in polyamide or sealed hermetically in glass jars with a polyamide layered plastic lid. The furnigated feed was stored for a maximum storage duration of 10 days during which loss was analyzed to be approximately 5%.		
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: The test substance was administered via fumigated diet. Feed mash was administered for a limited period (1 or 2 hours) twice a day at the same time each day. Consumption and concentration of the test substance was measured in effort to maintain consistency. It was not reported whether animals were trained to the limited feeding schedule prior to implementation.		

Continued on next page ...

HERO ID: 194588 Table: 2 of 3

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Study Citation:	Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111.
Health	Renal/Kidney; Hepatic/Liver;
Outcome(s):	
Reported Health	Renal/Kidney: serum urea, uric acid, glucose; Hepatic/Liver: liver fat content, serum total protein, cholesterol, ALT, AST;
Effect(s):	
<b>Duration:</b>	Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment during gestation, lactation-through weaning. Then females were returned to communal cages to repeat the treatment regimen for 5 pregnancies over 2 years
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
TIEDO ID	10.4500

Chemical: HEDO ID

HERO ID:	194588			
Domain		Metric	Rating	Comments
Domain	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Administered diet concentration (ppm) were reported. Diet was weighed (weekly) in order to determine amount consumed but those results were not reported. Feed was consumed primarily in the evening time frame with the majority during the first hour indicating the dose was consumed largely in a small time frame. Doses present in the diet after the 1-2h consumption period were reportedly 60-70% that of initially in mash and the authors stated, "since the amount eaten and the residue level were known, the amount of fumigant actually consumed was calculated with fair accuracy", therefore, it is implied that this was accounted for. It is unclear if the introduction of diet for limited time frames caused any initial changes in food consumption, thus altering the dose consumed, though the authors reported the animals "grew accustomed to consuming it quickly". It is unclear if the amount consumed is consistent to that consumed if feed were presented ad libitum. The doses could potentially be calculated.
	Metric 10:	Exposure Frequency and Duration	Uninformative	All Outcomes: Exposure frequency was 1-2 hours, twice daily, for 7 days/week differed from typical study design but was altered due to test substance volatility. Exposure duration appears to be intermittent: reported exposure for 6 weeks during premating, it was stated that during mating animals were on a control diet, and following mating (gestation- weaning) it was unclear if the treated diet was continued. After weaning, females were added to communal cages and it was implied that the intermittent exposure was repeated (for 4-5 pregnancies total). The uncertainty in exposure frequency, duration (2 years), and repeated matings were not consistent with guidelines for the study type (chronic).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: The number of exposure groups was limited to 2 treated groups and a control. Dose spacing did not encompass any effects therefore it is unclear whether spacing was appropriate.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The exposure method was not suited to the test substance. The test substance is volatile, and it was prepared in the diet. However, the authors attempted to mitigate the issues of volatility in feed via sealed fumigation, limited feeding times and

Domain 4: Test Animals

Continued on next page ...

monitoring of the test substance residues.

## Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111. Renal/Kidney; Hepatic/Liver;

**Outcome(s):** 

**Reported Health** 

Renal/Kidney: serum urea, uric acid, glucose; Hepatic/Liver: liver fat content, serum total protein, cholesterol, ALT, AST;

Effect(s):

Health

**Duration:** Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment

during gestation, lactation-through weaning. Then females were returned to communal cages to repeat the treatment regimen for 5 pregnancies over 2 years

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	194588	, , , , , , , , , , , , , , , , , , , ,		
Domain		Metric	Rating	Comments
	Metric 13:	Test Animal Characteristics	Low	Renal/Kidney: Animal characteristics were not completely reported. The details included the species (rats) and sex (male and female). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.; Hepatic/Liver: Animal characteristics were not completely reported. The details included the species (rats) and sex (female). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry conditions were not sufficiently reported to evaluate adequacy.
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals (18/group) were reported and were adequate for this study type.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The outcome assessment included serum chemistry only. The assessmen was sensitive but only partially addressed the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The outcome assessment was briefly described, previously cited and was carried out consistently across groups.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: In table 6 it was specified that clinical chemistry results were from groups of 4-5 females
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not necessary because this outcome of interest is not subjective in nature or is not required for this outcome of interest.
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control animals responded appropriately.
Domain 6: Confoundi	ng / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Information to determine confounding was not reported. No differences were identified from the reported information. With the measured residue of the test substance being 60-70% in feed after the feeding period (of 1-2 hours) it is possible that due to the volatility of the test substance, some was inhaled. Information regarding food consumption was insufficient so it is unclear whether the animals consumed an amount similar to that of feed presented ad libitum. It is unclear whether there were palatability issues (if there were, they may have been complicated by the intermittent feeding).
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	All Outcomes: It was reported that animals at 14 months and greater exhibited chronic respiratory disease- confirmed by necropsy that reduced survival. Additionally, reproduction ceased as animals aged.
		Coi	ntinued on next page .	

HERO ID: 194588 Table: 2 of 3

### ... continued from previous page

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111.

Health

Renal/Kidney; Hepatic/Liver;

**Outcome(s):** 

Reported Health

Renal/Kidney: serum urea, uric acid, glucose; Hepatic/Liver: liver fat content, serum total protein, cholesterol, ALT, AST;

Effect(s): Duration:

Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment during gestation, lactation-through weaning. Then females were returned to communal cages to repeat the treatment regimen for 5 pregnancies over 2 years

Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

Domain		Metric	Rating	Comments
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were used and reported as analysis of variance with
				Duncan multiple range test pairwise comparison. Significance was denoted in tables and
				figures. This is an appropriate method of analysis for the data type.
	Metric 24:	Reporting of Data	Medium	All Outcomes: The study data were reported in a table for each group and discussed in
				the text.

## **Overall Quality Determination**

## Uninformative

HERO ID: 194588 Table: 3 of 3

**Study Citation:** Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111. Health Reproductive/Developmental Outcome(s): fertility (no. mated, no. pregnant, no. with litters), litter size, litter survival, litter weights Reported Health Effect(s): **Duration:** Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment during gestation, lactation-through weaning. Then females were returned to communal cages to repeat the treatment regimen for 5 pregnancies over 2 years Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 194588 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High The test chemical was reported by name as ethylene dichloride (1,2 dichloroethane). CASRN was not reported. Metric 2: Test Substance Source High The test substance source was not reported; however, it was analytically verified by the laboratory. Metric 3: Test Substance Purity Low Purity of test substance was not reported. Domain 2: Test Design Metric 4: Negative and Vehicle Controls High The study included concurrent negative controls (implied unfumigated diet) and conditions were not explicitly stated but assumed to be consistent with the treated animals. Positive Controls N/A Metric 5: Positive controls are not required for this study type. Metric 6: Randomized Allocation of Animals Low There were no reported details on allocation or distribution of animals. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Medium The test substance preparation was as follows: feed was exposed to the test substance in hermetically sealed containers and stored in polyvinyl bags coated in polyamide or Substance sealed hermetically in glass jars with a polyamide layered plastic lid. The fumigated feed was stored for a maximum storage duration of 10 days during which loss was analyzed to be approximately 5%. Metric 8: Consistency of Exposure Medium The test substance was administered via fumigated diet. Feed mash was administered for a limited period (1 or 2 hours) twice a day at the same time each day. Consumption Administration and concentration of the test substance was measured in effort to maintain consistency. It was not reported whether animals were trained to the limited feeding schedule prior to implementation. Metric 9: Reporting of Doses/Concentrations Medium Administered diet concentration (ppm) were reported. Diet was weighed (weekly) in order to determine amount consumed but those results were not reported. Feed was consumed primarily in the evening time frame with the majority during the first hour indicating the dose was consumed largely in a small time frame. Doses present in the diet after the 1-2h consumption period were reportedly 60-70% that of initially in mash and the authors stated, "since the amount eaten and the residue level were known, the amount of fumigant actually consumed was calculated with fair accuracy", therefore, it is implied that this was accounted for. It is unclear if the introduction of diet for limited time frames caused any initial changes in food consumption, thus altering the dose consumed, though the authors reported the animals "grew accustomed to consuming it quickly". It is unclear if the amount consumed is consistent to that consumed if feed were presented ad libitum. The doses could potentially be calculated. Continued on next page ...

HERO ID: 194588 Table: 3 of 3

### ... continued from previous page

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food and Cosmetics Toxicology 14(2):105-111.

Health

Reproductive/Developmental

Outcome(s): Reported Health

th fertility (no. mated, no. pregnant, no. with litters), litter size, litter survival, litter weights

Effect(s): Duration:

Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment during gestation, lactation-through weaning. Then females were returned to communal cages to repeat the treatment regimen for 5 pregnancies over 2 years

Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERU ID:	194388			
Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	Uninformative	Exposure frequency was 1-2 hours, twice daily, for 7 days/week differed from typical study design but was altered due to test substance volatility. Exposure duration appears to be intermittent: reported exposure for 6 weeks during premating, it was stated that during mating animals were on a control diet, and following mating (gestation- weaning it was unclear if the treated diet was continued. After weaning, females were added to communal cages and it was implied that the intermittent exposure was repeated (for 4-5 pregnancies total). The uncertainty in exposure frequency and duration and the duration (2 years) and repeated matings were not suitable for the study type (repro dev) make this metric unacceptable.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	The number of exposure groups was limited to 2 treated groups and a control. Dose spacing did not encompass any effects therefore it is unclear whether spacing was appropriate.
	Metric 12:	Exposure Route and Method	Medium	The exposure method was not suited to the test substance. The test substance is volatile and it was prepared in the diet. However, the authors attempted to mitigate the issues of volatility in feed via sealed fumigation, limited feeding times and monitoring of the test substance residues.
Domain 4: Test Anir	nals			
	Metric 13:	Test Animal Characteristics	Low	Animal characteristics were not completely reported. The details included the species (rats) and sex (female). Strain, age and starting body were not reported. The source of animals was not specified for each study, however in one description, the authors stated "the rats used were bred locally" it is unclear if this applies to all animals.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not sufficiently reported to evaluate adequacy.
	Metric 15:	Number of Animals per Group	Medium	The number of animals (18/group) were reported and were adequate for this study type
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment included reproductive parameters. The assessment was sensitive for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The outcome assessment was briefly described, previously cited, and was carried out consistently across groups.
	Metric 18:	Sampling Adequacy	High	All animals were sampled for the outcome of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary because this outcome of interest is not subjective in nature or is not required for this outcome of interest.
	Metric 20:	Negative Control Response	High	Negative control animals responded appropriately.

1,1-Dichloroethane

### ... continued from previous page

Study Citation: Alumot, E., Nachtomi, E., Mandel, E., Holstein, P. (1976). Tolerance and acceptable daily intake of chlorinated furnigants in the rat diet. Food and

Cosmetics Toxicology 14(2):105-111.

Health Reproductive/Developmental

Outcome(s):

Reported Health

fertility (no. mated, no. pregnant, no. with litters), litter size, litter survival, litter weights

Effect(s):

**Duration:** Reproductive/Developmental Females, intermittent exposure: treated during 6 weeks premating, not treated during 10 d mating period, Unclear treatment

during gestation, lactation-through weaning. Then females were returned to communal cages to repeat the treatment regimen for 5 pregnancies over 2 years

HERO ID: 194588 Table: 3 of 3

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 194588

112110 121	17 1500					
Domain		Metric	Rating	Comments		
Domain 6: Confound	Confounding / Variable Control					
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Information to determine confounding was not reported. No differences were identified from the reported information. With the measured residue of the test substance being 60-70% in feed after the feeding period (of 1-2 hours) it is possible that due to the volatility of the test substance, some was inhaled. Information regarding food consumption was insufficient so it is unclear whether the animals consumed an amount similar to that of feed presented ad libitum. It is unclear whether there were palatability issues (if there were, they may have been complicated by the intermittent feeding).		
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	It was reported that animals at 14 months and greater exhibited chronic respiratory disease- confirmed by necropsy that reduced survival. Additionally, reproduction ceased as animals aged.		
	Metric 23:	Data Presentation and Analysis	Uninformative	The statistical analysis (ANOVA with Dunnett's test) was reported in the methods, however, for the pregnancies it is unclear whether statistical methods were applied to pregnancy 1 and then pregnancies 2-5 combined (in one analysis with n=66-72) or if each pregnancy was evaluated separately (which would be appropriate). There is also uncertainty whether the analysis was performed based on a per litter basis or individual animal basis. Finally, there is no variability reported for any of the repro parameters so statistics cannot be performed independently.		
	Metric 24:	Reporting of Data	Uninformative	Data reporting for the female repro endpoint is inconsistent. The results for pregnancy 1 (likely from the mating of exposed females with unexposed males, though this is unclear) are presented separately whereas the results from pregnancies 2-5 are combined and presented as totals (# pregnant, # with litters) or means (litter size, pup mortality and body weight) for all of these pregnancies taken together. Because these were repeated pregnancies, rather than individual pregnancies, this presentation of data is incorrect and misleading. The remaining pregnancies (6 and 7, with 6 presumably with exposed males and 7 with younger, unexposed males) are not reported at all.		

## **Overall Quality Determination**

## Uninformative

**Study Citation:** Lane, R.W., Riddle, B.L., Borzelleca, J.F. (1982). Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and develop-

ment in mice. Toxicology and Applied Pharmacology 63(3):409-421.

Health Reproductive/Developmental

**Outcome(s):** 

**Reported Health** Fertility, gestation, viability, litter size, sex ratio, pup weight gain and teratology

Effect(s):

**Duration:** Reproductive/Developmental multigenerational- 1,2-Dichloroethane

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments		
Domain 1: Test Substan						
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichloroethane.		
	Metric 2:	Test Substance Source	Low	The source of 1,2-dichloroethane was Aldrich Chemical Co, Milwaukee, Wis. The batch/lot number was not provided.		
	Metric 3:	Test Substance Purity	High	The purity was reported at 99+%.		
Domain 2: Test Design						
	Metric 4:	Negative and Vehicle Controls	High	Appropriate negative controls were used.		
	Metric 5:	Positive Controls	Low	For the dominant lethal portion of the study, OECD test guideline 478 requires inclusion of a positive control or demonstration of laboratory competence in this assay. The study authors report that "frequency of dominant lethal factors was minimal when compared to the results in females mated to males receiving 0.05 mg/ml cycophosphamide in drinking water 14 weeks, data not shown". Details of this positive control treatment or response were not further described.		
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated by computer into test groups.		
Domain 3: Exposure Ch	aracterization					
	Metric 7:	Preparation and Storage of Test Substance	High	Preparation and storage conditions of test substance was adequate.		
	Metric 8:	Consistency of Exposure	High	Exposure was consistent across study groups		
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Dose was calculated based on average fluid consumption for a 35-g mouse and not based on actual water consumed or weight of mouse. Nominal concentrations in water are not analytically confirmed. Concentrations in water were not analytically confirmed.		
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.		
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and doses administered were appropriate and based on acute LD50 data.		
	Metric 12:	Exposure Route and Method	High	Exposure route and method were appropriate.		
Domain 4: Test Animals	3					
	Metric 13:	Test Animal Characteristics	Medium	Initial body weights were not provided.		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported.		
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group were appropriate for outcomes studied.		
	Continued on next page					

HERO ID: 62609 Table: 1 of 2

#### ... continued from previous page

Study Citation: Lane, R.W., Riddle, B.L., Borzelleca, J.F. (1982). Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and develop-

ment in mice. Toxicology and Applied Pharmacology 63(3):409-421.

Data Presentation and Analysis

Reporting of Data

Health

Reproductive/Developmental

**Outcome(s):** 

Reported Health

Fertility, gestation, viability, litter size, sex ratio, pup weight gain and teratology

**Effect(s):** 

**Duration:** Reproductive/Developmental multigenerational- 1,2-Dichloroethane

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62609

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment and methodology were appropriate.
Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
Metric 18:	Sampling Adequacy	Low	The sampling was adequate for some outcomes of interest. In the dominant lethal study, OECD guidelines recommend including enough dams to produce at least 400 implants to provide sufficient power, but some groups produced fewer than 200 implants.
Metric 19:	Blinding of Assessors	N/A	Not necessary for this study design.
Metric 20:	Negative Control Response	Low	The fertility index of control animals appeared to be low relative to historical control ranges of 80-100 reported by Charles River (https://www.crj.co.jp/cms/crj/pdf/product/rm/information/icr/CRL_Reproductive_behavioral_evaluations_ICR_20 In litters F/1B and F2A, authors report fertility index of 70 and 76.2 in controls. In the dominant lethal study, the fertility index in controls was as low as 56.7. There were also some differences between naive control and vehicle controls for some endpoints.
Domain 6: Confounding / Variable Co	ontrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Not all potential confounders were reported. Authors state that there was no aversion (decreased fluid consumption) to either the vehicle or test substance.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	•		

Statistics analysis were performed and appropriate.

All outcome data was reported.

# **Overall Quality Determination**

Metric 23:

Metric 24:

# High

High

High

HERO ID: 62609 Table: 2 of 2

Study Citation: Lane, R.W., Riddle, B.L., Borzelleca, J.F. (1982). Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and develop-

ment in mice. Toxicology and Applied Pharmacology 63(3):409-421.

Health

Mortality; Nutritional/Metabolic;

**Outcome(s):** 

Reported Health

Mortality: Mortality of exposed adults; Nutritional/Metabolic: Body weight of F0 generation, fluid consumption;

**Effect(s):** 

**Duration:** Reproductive/Developmental multigenerational- 1,2-Dichloroethane

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	02009			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of 1,2-dichloroethane was Aldrich Chemical Co, Milwaukee,
				Wis. The batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity was reported at 99+%.
Domain 2: Test Design				
8	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Appropriate negative controls were used.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly allocated by computer into test groups.
				, , , ,
Domain 3: Exposure Ch				
	Metric 7:	Preparation and Storage of Test	High	All Outcomes: Preparation and storage conditions of test substance was adequate.
	Metric 8:	Substance	TT: _1_	All O ( ) F
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposure was consistent across study groups
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Dose was calculated based on average fluid consumption for a 35-g
		1 8		mouse and not based on actual water consumed or weight of mouse. Concentrations in
				water were not analytically confirmed.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and	High	All Outcomes: The number of exposure groups and doses administered were appropriate
		Dose/Concentration Spacing		and based on acute LD50 data.
	Metric 12:	Exposure Route and Method	High	All Outcomes: Exposure route and method were appropriate.
Domain 4: Test Animals	,			
Domain 4. 10st / miniais	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Initial body weights were not provided.
	Metric 14:	Adequacy and Consistency of Animal	High	All Outcomes: All husbandry conditions were reported.
		Husbandry Conditions	0	
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group were appropriate for outcomes studied.
D				
Domain 5: Outcome Ass		Outrous Assessment Mathed	TT: _L	
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment and methodology were appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: The sampling was adequate for the outcomes of interest.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this study design.
		Contin	nued on nex	at page

## Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

Study Citation: Lane, R.W., Riddle, B.L., Borzelleca, J.F. (1982). Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and development in mice. Toxicology and Applied Pharmacology 63(3):409-421.

Health Mortality; Nutritional/Metabolic;

**Outcome(s):** 

**Reported Health** Mortality: Mortality of

Effect(s):

Mortality: Mortality of exposed adults; Nutritional/Metabolic: Body weight of F0 generation, fluid consumption;

**Duration:** Reproductive/Developmental multigenerational- 1,2-Dichloroethane

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 62609

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	Medium	All Outcomes: There were differences between naive control and vehicle control. These differences are unlikely to substantially impact results.
Domain 6: Confound	ding / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Not all potential confounders were reported. Authors state that there was no aversion (decreased fluid consumption) to either the vehicle or test substance.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistics analysis were performed and appropriate.
	Metric 24:	Reporting of Data	High	All Outcomes: All outcome data was reported.

# Overall Quality Determination High

Human Health Hazard Animal Toxicology Evaluation

Study Citation: Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of

1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198.

Health Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** Maternal body weights

Effect(s):

**Duration:** Reproductive/Developmental GD 6-20- inhalation **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substance	ce			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichloroethane; CASRN 107-06-2.
	Metric 2:	Test Substance Source	High	The test substance sources were clearly reported. The unlabeled test substance was purchased from Merck.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was acceptable (>99%).
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Concurrent negative controls were exposed to filtered room air only.
	Metric 5:	Positive Controls	N/A	Positive controls not required for this type of study
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups. Normalization to body weights was not specified.
Domain 3: Exposure Ch	aracterization			
	Metric 7:	Preparation and Storage of Test Substance	High	The equipment and methods used for vapor generation were appropriate and clearly described.
	Metric 8:	Consistency of Exposure Administration	Low	The chamber designs were consistent across groups. The time of day of exposure and the number of animals per cage was not specified. This missing information could have a significant impact on the results of the study.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The study reported both target and analytical concentrations of the test substance. Air samples were analyzed continuously by gas-liquid chromatography and men time-weighted average analytical concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed for 6 hrs/day from GD 6 to 20. The exposure window was appropriate and sensitive for the outcomes of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included four exposure groups. The concentrations were not explicitly justified by the study authors; however, the concentrations selected were within the ranges reported in other studies referenced in the introduction. This includes one that reported severe maternal toxicity in rats exposed to 300 ppm, which was selected as the high concentration in this study.
	Metric 12:	Exposure Route and Method	Medium	Animals were exposed whole body to the vaporized test substance. It was not specified whether vapors condensed on animal fur at the high concentrations. The number of air changes was not stated for the dynamic air chamber.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, source, parity, and starting body weights were reported. The age of the animals was not reported.

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Study Citation:	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198.					
Health	Nutritional/Metabolic					
Outcome(s):						
Reported Health	Maternal body weights					
Effect(s):						
Duration:	Reproductive/Developmental GD 6-20- inhalation					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	12099					
Domain		Metric	Rating	Comments		
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some animal husbandry details were provided. Room temperature, humidity, and light cycle were specified and were consistent across groups. Details on animal caging and bedding were not mentioned. Food and water were available ad libitum, except during inhalation exposures. The number of animals per cage was not specified.		
	Metric 15:	Number of Animals per Group	Medium	The study used 26 pregnant females per group which is acceptable for this type of study.		
Domain 5: Outcome A	Assessment Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodologies were clearly reported and were appropriate and sensitive to the outcomes of interest.		
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported. The outcomes were consistently addressed across exposure groups.		
	Metric 18:	Sampling Adequacy	High	Sampling included all dams pregnant at euthanization. The sampling was adequate for the outcome of interest.		
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for simple measurements such as body weights.		
	Metric 20:	Negative Control Response	High	The negative control responses were reported and were appropriate.		
Domain 6: Confoundi	na / Variable Co	ntral				
Domain o. Comoundi	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report all information to determine confounding (e.g., food and water intake, respiratory rates), and 1,2-DCE is a respiratory irritant.		
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Two deaths occurred in the high-exposure group. The causes of death were not reported, and it is unclear whether the deaths were exposure related, or due to a health outcome unrelated to exposure. Because only a small number of animals died, this is not likely to have a substantial impact on the outcome assessment.		
	Metric 23:	Data Presentation and Analysis	High	Statistical methods used in the study were adequately reported and were appropriate for the dataset.		
	Metric 24:	Reporting of Data	High	The data for each exposure group were quantitatively reported as means $\pm$ SEM.		

## **Overall Quality Determination**

## High

Study Citation:	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198.
Health	Mortality
Outcomo(a)	. To tunity

**Outcome(s):** 

**Reported Health** 

Maternal death (GD 6-20 oral and inhalation)

Effect(s):

**Duration:** Reproductive/Developmental GD 6-20- inhalation Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substanc	e			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichloroethane; CASRN 107-06-2.
	Metric 2:	Test Substance Source	High	The test substance sources were clearly reported. The unlabeled test substance was purchased from Merck.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was acceptable (>99%).
Domain 2: Test Design				
Č	Metric 4:	Negative and Vehicle Controls	High	Concurrent negative controls were exposed to filtered room air only.
	Metric 5:	Positive Controls	N/A	Positive controls not required for this type of study
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups. Normalization to body weights was not specified.
Domain 3: Exposure Cha	racterization			
•	Metric 7:	Preparation and Storage of Test Substance	High	The equipment and methods used for vapor generation were appropriate and clearly described.
	Metric 8:	Consistency of Exposure Administration	Low	Chamber designs were consistent across groups. The time of day of exposure and the number of animals per cage was not specified. This missing information could have a significant impact on the results of the study.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The study reported both target and analytical concentrations of the test substance. Air samples were analyzed continuously by gas-liquid chromatography and men time-weighted average analytical concentrations were reported.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed for 6 hrs/day from GD 6 to 20. The exposure window was appropriate and sensitive for the outcomes of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included four exposure groups. The concentrations were not explicitly justified by the study authors; however, the concentrations selected were within the ranges reported in other studies referenced in the introduction. This includes one that reported severe maternal toxicity in rats exposed to 300 ppm, which was selected as the high concentration in this study.
	Metric 12:	Exposure Route and Method	Medium	Animals were exposed whole body to the vaporized test substance. It was not specified whether vapors condensed on animal fur at the high concentrations. The number of air changes was not stated for the dynamic air chamber.
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, source, parity, and starting body weights were re-
		2001 I III III Characterishes	. ricaram	ported. The age of the animals was not reported.

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Study Citation:	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198.						
Health	Mortality						
Outcome(s):							
Reported Health Effect(s):	Maternal dea	ath (GD 6-20 oral and inhalation)					
<b>Duration:</b>	Reproductive	e/Developmental GD 6-20- inhalation					
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane					
HERO ID:	12099						
Domain		Metric	Rating	Comments			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some animal husbandry details were provided. Room temperature, humidity, and light cycle were specified and were consistent across groups. Details on animal caging and bedding were not mentioned. Food and water were available ad libitum, except during inhalation exposures. The number of animals per cage was not specified.			
	Metric 15:	Number of Animals per Group	Medium	The study used 26 pregnant females per group which is acceptable for this type of study.			
Domain 5: Outcome		Outcome Accessorat Make Jelese	M - J:				
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodologies were not clearly reported, but based on the results, maternal animals were monitored for mortality, and the results were reported.			
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of the outcome assessment protocol were not provided, but for the mortality outcome, this is not expected to have a significant impact on the study results. There is no indication that there were inconsistencies in the assessment across groups.			
	Metric 18:	Sampling Adequacy	High	All animals per group were assessed for this outcome of interest.			
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for subjective outcomes.			
	Metric 20:	Negative Control Response	High	The negative control responses were reported and were appropriate.			
Domain 6: Confound	ing / Variable Coi	ntrol					
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report all information to determine confounding (e.g., food and water intake, respiratory rates), and 1,2-DCE is a respiratory irritant.			
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Two deaths occurred in the high-exposure group. The causes of death were not reported, and it is unclear whether the deaths were exposure related, or due to a health outcome unrelated to exposure. Because only a small number of animals died, this is not likely to have a substantial impact on the outcome assessment.			
	Metric 23:	Data Presentation and Analysis	High	Statistical methods used in the study were adequately reported. Incidence data were provided allowing for an independent analysis.			
	Metric 24:	Reporting of Data	High	Incidences of maternal mortality were clearly reported.			
Overall Qual	lity Detern	nination	High				

HERO ID: 12099 Table: 3 of 6

Study Citation:  Health Outcome(s):	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198. Reproductive/Developmental							
Reported Health Effect(s):	Maternal toxicity, pregnancy outcomes and fetal external, skeletal, and visceral examinations (oral and inhalation, GD6-20)							
Duration: Chemical: HERO ID:		e/Developmental GD 6-20- inhalation pethane- Isomer: 1,2-Dichloroethane						
Domain		Metric	Rating	Comments				
Domain 1: Test Substan								
	Metric 1: Metric 2:	Test Substance Identity Test Substance Source	High High	The test substance was identified as 1,2-dichloroethane; CASRN 107-06-2.  The test substance sources were clearly reported. The unlabeled test substance was purchased from Merck.				
	Metric 3:	Test Substance Purity	High	The purity of the test substance was acceptable (>99%).				
Domain 2: Test Design								
	Metric 4: Metric 5:	Negative and Vehicle Controls Positive Controls	High N/A	Concurrent negative controls were exposed to filtered room air only.				
	Metric 6:	Randomized Allocation of Animals	Low	Positive controls not required for this type of study  The study did not report how animals were allocated into study groups. Normalization to body weights was not specified.				
D Ch								
Domain 3: Exposure Ch	aracterization Metric 7:	Preparation and Storage of Test	High	The equipment and methods used for vapor generation were appropriate and clearly				
	Wictire 7.	Substance	High	described.				
	Metric 8:	Consistency of Exposure Administration	Low	The chamber designs were consistent across groups. The time of day of exposure and the number of animals per cage was not specified. This missing information could have a significant impact on the results of the study.				
	Metric 9:	Reporting of Doses/Concentrations	Medium	The study reported both target and analytical concentrations of the test substance. Air samples were analyzed continuously by gas-liquid chromatography and men time-weighted average analytical concentrations were reported.				
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were exposed for 6 hrs/day from GD 6 to 20. The outcomes in this study included pregnancy rate, and number of implantations; however, dosing did not begin until after implantation occurred (GD6). Other outcomes included an assessment of visceral and skeletal anomalies, and the exposure frequency and duration were appropriate for these outcomes.				
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included four exposure groups. The concentrations were not explicitly justified by the study authors; however, the concentrations selected were within the ranges reported in other studies referenced in the introduction. This includes one that reported severe maternal toxicity in rats exposed to 300 ppm, which was selected as the high concentration in this study.				
	Metric 12:	Exposure Route and Method	Medium	Animals were exposed whole body to the vaporized test substance. It was not specified whether vapors condensed on animal fur at the high concentrations.				
Domain 4: Test Animals	3							
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Study Citation: Health	1,2-dichloro	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198. Reproductive/Developmental							
Outcome(s): Reported Health Effect(s):	Maternal tox	Maternal toxicity, pregnancy outcomes and fetal external, skeletal, and visceral examinations (oral and inhalation, GD6-20)							
Duration: Chemical: HERO ID:		e/Developmental GD 6-20- inhalation bethane- Isomer: 1,2-Dichloroethane							
Domain		Metric	Rating	Comments					
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, source, parity, and starting body weights were reported. The age of the animals was not reported.					
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some animal husbandry details were provided. Room temperature, humidity, and light cycle were specified and were consistent across groups. Details on animal caging and bedding were not mentioned. Food and water were available ad libitum, except during inhalation exposures. The number of animals per cage was not specified.					
	Metric 15:	Number of Animals per Group	Medium	The study used 26 pregnant females per group which is acceptable for this type of study.					
Domain 5: Outcome									
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodologies were clearly reported and were appropriate and sensitive to the outcomes of interest.					
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported. The outcomes were consistently addressed across exposure groups.					
	Metric 18:	Sampling Adequacy	High	The sample sizes were clearly reported and were appropriate to adequately assess the outcomes of interest.					
	Metric 19:	Blinding of Assessors	N/A	The study did not report blinding; however, blinding is not required for non-subjective outcomes, or simple measures, and is not required for assessment of fetal anomalies					
	Metric 20:	Negative Control Response	High	The negative control responses were reported and were appropriate.					
Domain 6: Confound	ing / Variable Co	ntrol							
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The study did not report all information to determine confounding (e.g., food and water intake, respiratory rates), and 1,2-DCE is a respiratory irritant.					
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Two deaths occurred in the high-exposure group. The causes of death were not reported, and it is unclear whether the deaths were exposure related, or due to a health outcome unrelated to exposure. Because only a small number of animals died, this is not likely to have a substantial impact on the outcome assessment.					
	Metric 23:	Data Presentation and Analysis	High	Statistical methods used in the study were adequately reported and were appropriate for the data. The litter was used as the basis of analysis where appropriate.					
	Metric 24:	Reporting of Data	High	All of the data were quantitatively reported as incidences or means $\pm$ SEM where appropriate. Individual animal data were not provided in this published report.					
Overall Qual	lity Detern	nination	High						

HERO ID: 12099 Table: 4 of 6

**Study Citation:** Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198. Mortality Health **Outcome(s): Reported Health** Maternal death (GD 6-20 oral and inhalation) Effect(s): Reproductive/Developmental GD6-20 - oral **Duration:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **Chemical:** 

**HERO ID:** 12099

Domain		Metric	Rating	Comments
Domain 1: Test Subst	tance			
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichloroethane; CASRN 107-06-2.
	Metric 2:	Test Substance Source	High	The test substance sources were clearly reported. The unlabeled test substance was purchased from Merck.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was acceptable (>99%).
Domain 2: Test Desig	gn			
	Metric 4:	Negative and Vehicle Controls	High	Concurrent negative controls were exposed to filtered room air only.
	Metric 5:	Positive Controls	N/A	Positive controls not required for this type of study
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups. Normalization to body weights was not specified.
Domain 3: Exposure	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Low	Details on the preparation of the test solutions were not described (e.g., homogeneity, frequency of preparation). Storage conditions were not specified, and the stability of the test substance was not addressed. The test substance is volatile in nature and the missing details may have a significant impact on the study results.
	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were generally reported and were consistent across groups. All animals were administered a gavage volume of 2 mL/kg bw. The time of day that animals were gavaged was not specified.
	Metric 9:	Reporting of Doses/Concentrations	High	The study reported nominal doses (in mmol/kg) based on the volume administered 2 mL/kg BW, and body weight measurements taken on GD6. The authors noted that "Corrections in dosage based on change in body weight during gestation would have contributed minimally (no more than 13%) to differences between actual exposure and calculated exposure (ie., 2.4 mM for GD 21 could have been as low as 2.2 mM).
	Metric 10:	Exposure Frequency and Duration	High	Animals were gavaged daily from GD 6 to 20. The exposure window was appropriate and sensitive for the outcome of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included four exposure groups. The concentrations were not explicitly justified by the study authors; however, the concentrations selected were within the ranges reported in other studies referenced in the introduction. This includes one that reported severe maternal toxicity in rats exposed to 300 ppm, which was selected as the high concentration in this study. The dose spacing was appropriate and allowed for NOAEL and LOAEL determinations for at least one endpoint.
	Metric 12:	Exposure Route and Method	High	Animals were exposed via gavage in corn oil. The route of exposure was appropriate for the test substance.

Domain 4: Test Animals

# July 2024 Human Health Hazard Animal Toxicology Evaluation

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Study Citation:	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198.							
Health	Mortality	-						
Outcome(s):								
Reported Health Effect(s):	Maternal dea	ath (GD 6-20 oral and inhalation)						
Duration:	Reproductive	e/Developmental GD6-20 - oral						
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane						
HERO ID:	12099							
Domain		Metric	Rating	Comments				
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, source, parity, and starting body weights were reported. The age of the animals was not reported.				
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some animal husbandry details were provided. Room temperature, humidity, and light cycle were specified and were consistent across groups. Details on animal caging and bedding were not mentioned. Food and water were available ad libitum. The number of animals per cage was not specified.				
	Metric 15:	Number of Animals per Group	Medium	The study used 26 pregnant females per group which is acceptable for this type of study.				
Domain 5: Outcome A	ssessment Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodologies were not clearly reported, but based on the results, maternal animals were monitored for mortality, and the results were reported.				
	Metric 17:	Consistency of Outcome Assessment	Medium	Details of the outcome assessment protocol were not provided, but for the mortality outcome, this is not expected to have a significant impact on the study results. There is no indication that there were inconsistencies in the assessment across groups.				
	Metric 18:	Sampling Adequacy	High	All animals per group were assessed for this outcome of interest.				
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for subjective outcomes.				
	Metric 20:	Negative Control Response	High	The negative control responses were reported and were appropriate.				
Domain 6: Confoundir	ng / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding (e.g., food and water intake)				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.				
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not necessary (no animals died)				
	Metric 24:	Reporting of Data	High	Maternal mortality results were clearly reported.				

## **Overall Quality Determination**

## High

Study Citation:	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of
Study Charlon.	Tayan, 3.1., Sameman, 7.1.1., Donnet, 1., 1 abiy, 3.1., Eangoine, 1., Sabate, 3.1. (1773). Assessment of the developmental toxicity and placental transfer of

1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198. **Health** Nutritional/Metabolic

**Outcome(s):** 

Reported Health

Maternal body weights

Effect(s):

**Duration:**Reproductive/Developmental GD6-20 - oral**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 12099

Domain		Metric	Rating	Comments
Domain 1: Test Substance				
I	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichloroethane; CASRN 107-06-2.
1	Metric 2:	Test Substance Source	High	The test substance sources were clearly reported. The unlabeled test substance was purchased from Merck.
1	Metric 3:	Test Substance Purity	High	The purity of the test substance was acceptable (>99%).
Domain 2: Test Design				
ı	Metric 4:	Negative and Vehicle Controls	High	Concurrent negative controls were administered an equal volume of corn oil.
I	Metric 5:	Positive Controls	N/A	Positive controls not required for this type of study
1	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups. Normalization to body weights was not specified.
Domain 3: Exposure Chara	acterization			
_	Metric 7:	Preparation and Storage of Test Substance	Low	Details on the preparation of the test solutions were not described (e.g., homogeneity, frequency of preparation). Storage conditions were not specified, and the stability of the test substance was not addressed. The test substance is volatile in nature and the missing details may have a significant impact on the study results.
I	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were generally reported and were consistent across groups. All animals were administered a gavage volume of 2 mL/kg bw. The time of day that animals were gavaged was not specified.
ī	Metric 9:	Reporting of Doses/Concentrations	Medium	The study reported nominal doses (in mmol/kg) based on the volume administered 2 mL/kg BW, and body weight measurements taken on GD6. The authors noted that "Corrections in dosage based on change in body weight during gestation would have contributed minimally (no more than 13%) to differences between actual exposure and calculated exposure (ie., 2.4 mM for GD 21 could have been as low as 2.2 mM).
I	Metric 10:	Exposure Frequency and Duration	High	Animals were gavaged daily from GD 6 to 20. The exposure window was appropriate and sensitive for the outcome of interest.
ī	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included four exposure groups. The concentrations were not explicitly justified by the study authors; however, the concentrations selected were within the ranges reported in other studies referenced in the introduction. This includes one that reported severe maternal toxicity in rats exposed to 300 ppm, which was selected as the high concentration in this study. The dose spacing was appropriate and allowed for NOAEL and LOAEL determinations for at least one endpoint.
1	Metric 12:	Exposure Route and Method	High	Animals were exposed via gavage in corn oil. The route of exposure was appropriate for the test substance.

Domain 4: Test Animals

Health Nutritional/Metabolic Series 28(2):187-198. Health Nutritional/Metabolic Outcome(s):  Reported Health Maternal body weights Effect(s):  Duration: Reproductive/Developmental GD6-20 - oral Chemical: 1,1-Dichlorocethane 12099  Domain (1,1-Dichlorocethane 12099  Domain (1,1-Dichlorocethane 12099  Domain (1,1-Dichlorocethane 12099  Metric 13: Test Animal Characteristics Medium Husbandry Conditions Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Series S			contin	ued from p	revious page			
Outcome(s): Reported Health Maternal body weights Effect(s): Duration: Reproductive/Developmental GD6-20 - oral Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane HERO ID: 12099  Domain Metric 13: Test Animal Characteristics Medium Husbandry Conditions Developmental Developmental Characteristics Medium Husbandry Conditions Developmental Developmental Developmental Characteristics Medium Husbandry Conditions Developmental Devel	-							
Reported Health Effect(s):  Duration: Reproductive/Developmental GD6-20 - oral Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane HERO ID: 12099  Domain Metric 13: Test Animal Characteristics Medium Husbandry Conditions Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Metric 15: Number of Animals per Group Medium Heric 15: Number of Animals per Group Medium Metric 16: Outcome Assessment Metric 17: Consistency of Outcome Assessment Methodology Metric 18: Sampling Adequacy Metric 19: Blinding of Assessors Metric 19: Blinding of Assessors Metric 20: Negative Control Response Metric 21: Confounding Variables in Test Design and Procedures Metric 23: Data Presentation and Analysis Metric 23: Data Presentation and Analysis Metric 24: Reporting of Data Metric 26: Satisfica methodos used in the study were adequated to recommendate of consported and were appropriate the dataset.  Metric 23: Data Presentation and Analysis Metric 24: Reporting of Data Metric 25: Data Presentation and Analysis Metric 24: Reporting of Data Metric 24: Reporting of Data Metric 25: Data Presentation and Analysis Metric 25: Data Presentation and Analysis Metric 26: Reporting of Data Metric 27: The data for each exposure group were quantitatively reported and were appropriate the dataset.  Metric 24: Reporting of Data Medium The study did not report all information to determine confounding (e.g., food and we intake) Medium The study did not report all information to determine confounding (e.g., food and we intake) Medium The study did not report all information in the least outcome assessment.  Metric 25: Data Presentation and Analysis Medium The study did not report all informatio		1 (difficility)	victasone.					
Domain   Domain   Metric 13: Test Animal Characteristics   Medium   The test animal species, strain, sex, source, parity, and starting body weights were reported. The age of the animals was not reported. The sex not reported and were consistent across groups.  Domain 5: Outcome Assessment  Metric 17: Consistency of Outcome Assessment High  Metric 28: Sampling Adequacy  Metric 29:	Reported Health	Maternal boo	dy weights					
Domain   Metric 13: Test Animal Characteristics   Medium   The test animal species, strain, sex, source, parity, and starting body weights were reported. The age of the animals was not reported. The	Duration:	Reproductive	e/Developmental GD6-20 - oral					
Domain	Chemical:	1,1-Dichloro	pethane- Isomer: 1,2-Dichloroethane					
Metric 13: Test Animal Characteristics Medium Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Medium High Husbandry Conditions  Medium High Husbandry Conditions  Medium Husbandry Conditions  Medium Husbandry Conditions  Medium High Husbandry Conditions  Medium Husbandry Conditions  Medium Husbandry Conditions  Medium High Husbandry Conditions  Medium High Husbandry Conditions  Medium Husbandry Conditions  High High High High High High High Hig	HERO ID:	12099						
Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group  Medium  Medium  Medium  Metric 15: Number of Animals per Group  Medium  Me	Domain		Metric	Rating	Comments			
Husbandry Conditions  Wetric 15: Number of Animals per Group  Medium  The study used 26 pregnant females per group which is acceptable for this type of some assessment methodologies were clearly reported and were adequate a sensitive for the outcome assessment methodologies were clearly reported and were adequate a sensitive for the outcome of interest.  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  High  Sampling included all dams pregnant at euthanization. The sampling was adequate the outcome of interest.  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Metric 20: Negative Control Response  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  High  The data for each exposure group were quantitatively reported as means ± SEM.		Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, source, parity, and starting body weights were reported. The age of the animals was not reported.			
Domain 5: Outcome Assessment  Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Metric 21: Confounding Variable Control  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  Metric 24: Reporting of Data  Metric 24: Reporting of Data  Metric 16: Outcome Assessment Methodology  High  The outcome assessment methodologies were clearly reported and were adequate a sensitive for the outcome of interest.  Details of the outcome assessment protocol were reported and animals were consist assessed across groups.  N/A Blinding is not required for simple measures.  M/A Blinding is not required for simple measures.  Medium The study did not report all information to determine confounding (e.g., food and were appropriate).  The study did not report all information to determine confounding (e.g., food and were differences among groups in animal attrition or health outcomes unrelated to expose (e.g., infection) that could influence the outcome assessment.  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  High  The data for each exposure group were quantitatively reported as means ± SEM.		Metric 14:		Medium	Some animal husbandry details were provided. Room temperature, humidity, and light cycle were specified and were consistent across groups. Details on animal caging and bedding were not mentioned. Food and water were available ad libitum. The number of animals per cage was not specified.			
Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Metric 20: Negative Control Response  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  Metric 24: Reporting of Data  Metric 26: Doutcome Assessment Methodology  High The outcome assessment methodologies were clearly reported and were adequate a sensitive for the outcome assessment protocol were reported and animals were consist assessed across groups.  Details of the outcome assessment protocol were reported and animals were consist assessed across groups.  Medium of the outcome assessment protocol were reported and animals were consist assessed across groups.  Medium of the outcome of interest.  Medium of the outcome assessment protocol were reported and animals were consist assessed across groups.  Medium of the outcome assessment protocol were reported and enthality assessment assessed across groups.  Medium of the outcome of interest.  Medium of the outcome of in		Metric 15:	Number of Animals per Group	Medium	The study used 26 pregnant females per group which is acceptable for this type of study.			
Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  Metric 21: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design  Metric 22: Health Outcomes Unrelated to  Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  Metric 24: Reporting of Data  Metric 26: Sampling Adequacy  High Sampling included all dams pregnant at euthanization. The sampling was adequate the outcome of interest.  N/A Blinding is not required for simple measures.  Melind The negative control responses were reported and were appropriate.  The negative control responses were reported and were appropriate.  The study did not report all information to determine confounding (e.g., food and we intake)  Medium The study did not report all information to determine confounding (e.g., food and we intake)  There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to expose (e.g., infection) that could influence the outcome assessment.  Metric 23: Data Presentation and Analysis  High The data for each exposure group were quantitatively reported as means ± SEM.	Domain 5: Outcome		Outcome Assessment Methodology	High	The outcome assessment methodologies were clearly reported and were adequate and sensitive for the outcome of interest.			
the outcome of interest.  Metric 19: Blinding of Assessors Metric 20: Negative Control Response  Metric 20: Negative Control Response  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  Metric 24: Reporting of Data  Metric 26: Negative Control Response  Medium The study did not report all information to determine confounding (e.g., food and wintake)  Medium There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to expose (e.g., infection) that could influence the outcome assessment.  Metric 24: Reporting of Data  High The data for each exposure group were quantitatively reported as means ± SEM.		Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and animals were consistently			
Metric 20: Negative Control Response High The negative control responses were reported and were appropriate.  Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  Metric 25: Negative Control Response  High The negative control responses were reported and were appropriate.  The study did not report all information to determine confounding (e.g., food and we intake)  Medium There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.  Metric 24: Reporting of Data  High The data for each exposure group were quantitatively reported as means ± SEM.		Metric 18:	Sampling Adequacy	High	Sampling included all dams pregnant at euthanization. The sampling was adequate for the outcome of interest.			
Domain 6: Confounding / Variable Control  Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  Medium The study did not report all information to determine confounding (e.g., food and wintake)  Medium There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposive (e.g., infection) that could influence the outcome assessment.  Metric 24: Reporting of Data  High The data for each exposure group were quantitatively reported as means ± SEM.		Metric 19:	Blinding of Assessors	N/A	Blinding is not required for simple measures.			
Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  Medium The study did not report all information to determine confounding (e.g., food and wintake)  There was no information either to support or dismiss the suggestion that there wer differences among groups in animal attrition or health outcomes unrelated to expos (e.g., infection) that could influence the outcome assessment.  Statistical methods used in the study were adequately reported and were appropriate the dataset.  Metric 24: Reporting of Data  High The data for each exposure group were quantitatively reported as means ± SEM.		Metric 20:	Negative Control Response	High	The negative control responses were reported and were appropriate.			
Metric 21: Confounding Variables in Test Design and Procedures  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis  Metric 24: Reporting of Data  Medium The study did not report all information to determine confounding (e.g., food and wintake)  There was no information either to support or dismiss the suggestion that there wer differences among groups in animal attrition or health outcomes unrelated to expos (e.g., infection) that could influence the outcome assessment.  Statistical methods used in the study were adequately reported and were appropriate the dataset.  Metric 24: Reporting of Data  High The data for each exposure group were quantitatively reported as means ± SEM.	Domain 6: Confound	ling / Variable Co	ntral					
Metric 22: Health Outcomes Unrelated to Exposure  Medium There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to expose (e.g., infection) that could influence the outcome assessment.  Metric 23: Data Presentation and Analysis  High Statistical methods used in the study were adequately reported and were appropriate the dataset.  Metric 24: Reporting of Data  High The data for each exposure group were quantitatively reported as means ± SEM.	Domain o. Comound	-	Confounding Variables in Test Design	Medium	The study did not report all information to determine confounding (e.g., food and water			
Metric 23: Data Presentation and Analysis  High Statistical methods used in the study were adequately reported and were appropriate the dataset.  Metric 24: Reporting of Data  High Statistical methods used in the study were adequately reported and were appropriate the dataset.  The data for each exposure group were quantitatively reported as means ± SEM.		Metric 22:	Health Outcomes Unrelated to	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure			
		Metric 23:	Data Presentation and Analysis	High	Statistical methods used in the study were adequately reported and were appropriate for			
		Metric 24:	Reporting of Data	High	The data for each exposure group were quantitatively reported as means $\pm$ SEM.			
Overall Quality Determination High	Overall One	lity Deterr	nination	High				

Study Citation:	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of
	1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198.

Health

Reproductive/Developmental

**Outcome(s):** 

**Reported Health** 

Maternal toxicity, pregnancy outcomes and fetal external, skeletal, and visceral examinations (oral and inhalation, GD6-20)

Effect(s):

**Duration:**Reproductive/Developmental GD6-20 - oral**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substan				
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichloroethane; CASRN 107-06-2.
	Metric 2:	Test Substance Source	High	The test substance sources were clearly reported. The unlabeled test substance was purchased from Merck.
	Metric 3:	Test Substance Purity	High	The purity of the test substance was acceptable (>99%).
Domain 2: Test Design				
Č	Metric 4:	Negative and Vehicle Controls	High	Concurrent negative controls were administered an equal volume of corn oil.
	Metric 5:	Positive Controls	N/A	Positive controls not required for this type of study
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups. Normalization to body weights was not specified.
Domain 3: Exposure Ch				
	Metric 7:	Preparation and Storage of Test Substance	Low	Details on the preparation of the test solutions were not described (e.g., homogeneity, frequency of preparation). Storage conditions were not specified, and the stability of the test substance was not addressed. The test substance is volatile in nature and the missing details may have a significant impact on the study results.
	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were generally reported and were consistent across groups. All animals were administered a gavage volume of 2 mL/kg bw. The time of day that animals were gavaged was not specified.
	Metric 9:	Reporting of Doses/Concentrations	Medium	The study reported nominal doses (in mmol/kg) based on the volume administered 2 mL/kg BW, and body weight measurements taken on GD6. The authors noted that "Corrections in dosage based on change in body weight during gestation would have contributed minimally (no more than 13%) to differences between actual exposure and calculated exposure (ie., 2.4 mM for GD 21 could have been as low as 2.2 mM).
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were gavaged daily from GD 6 to 20. The outcomes in this study included pregnancy rate, and number of implantations; however, dosing did not begin until after implantation occurred (GD6). Other outcomes included an assessment of visceral and skeletal anomalies, and the exposure frequency and duration were appropriate for these outcomes.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included four exposure groups. The concentrations were not explicitly justified by the study authors; however, the concentrations selected were within the ranges reported in other studies referenced in the introduction. This includes one that reported severe maternal toxicity in rats exposed to 300 ppm, which was selected as the high concentration in this study. The dose spacing was appropriate and allowed for NOAEL and LOAEL determinations for at least one endpoint.

### Human Health Hazard Animal Toxicology Evaluation

### ... continued from previous page

Study Citation:	Payan, J.P., Saillenfait, A.M., Bonnet, P., Fabry, J.P., Langonne, I., Sabate, J.P. (1995). Assessment of the developmental toxicity and placental transfer of
	1,2-dichloroethane in rats, Toxicological Sciences 28(2):187-198.

Health

Reproductive/Developmental

Outcome(s): Reported Health

Maternal toxicity, pregnancy outcomes and fetal external, skeletal, and visceral examinations (oral and inhalation, GD6-20)

Effect(s):

Duration:Reproductive/Developmental GD6-20 - oralChemical:1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 12099

HERO ID.	12000			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	High	Animals were exposed via gavage in corn oil. The route of exposure was appropriate for the test substance.
Domain 4: Test Animals	S			
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, source, parity, and starting body weights were reported. The age of the animals was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some animal husbandry details were provided. Room temperature, humidity, and light cycle were specified and were consistent across groups. Details on animal caging and bedding were not mentioned. Food and water were available ad libitum. The number of animals per cage was not specified.
	Metric 15:	Number of Animals per Group	Medium	The study used 26 pregnant females per group which is acceptable for this type of study
Domain 5: Outcome Ass	sessment			
Domain 3. Outcome 715.	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodologies were clearly reported and were adequate and sensitive for the outcome of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and animals were consistently assessed across groups.
	Metric 18:	Sampling Adequacy	High	The sample sizes were clearly reported and were appropriate to adequately assess the outcomes of interest.
	Metric 19:	Blinding of Assessors	N/A	The study did not report blinding; however, blinding is not required for non-subjective outcomes, or simple measures, and is not required for assessment of fetal anomalies.
	Metric 20:	Negative Control Response	High	The negative control responses were reported and were appropriate.
Domain 6: Confounding	r / Variable Co	ntral		
Domain o. Comounting	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding (e.g., food and water intake)
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods used in the study were adequately reported and were appropriate for the data. The litter was used as the basis of analysis where appropriate.
	Metric 24:	Reporting of Data	High	The data for each exposure group were quantitatively reported as incidences or means $\pm$ SEM.

## **Overall Quality Determination**

High

Animal Toxicology Evaluation	HERO ID: 5/153530 Table: 1 of /

Study Citation:	Rao, K.S., Murray, J.S., Deacon, M.M., John, J.A., Calhoun, L.L., Young, J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylene
Health	dichloride. 5:P149-P166. Mortality; Reproductive/Developmental;
Outcome(s):	· ··· · · · · · · · · · · · · · · · ·
Reported Health	Mortality: Mortality: Reproductive/Developmental: Developmental Rat Study: Number of corpora lutea, number and position of live, dead and resorbed

Reported Health Effect(s):

Mortality: Mortality; Reproductive/Developmental: Developmental Rat Study:Number of corpora lutea, number and position of live, dead and resorbed fetuses and fetal weight, length, sex, external alteration, skeletal alteration, and cleft palate. Developmental Rabbit Study: Number of corpora lutea, number and position of live, dead and resorbed fetuses and fetal weight, length, sex, external alteration, skeletal alteration, and cleft palate. Reproductive Study in Rats: Fertility index, gestation days, sex ratio, neonatal body weight, gestation survival index, gross pathological examination of pups. Histology on ovaries, uterus and testes.;

**Duration:**Reproductive/Developmental Developmental**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Subs	tance			
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as ethylene dichloride (1,2-dichlroethane).
	Metric 2:	Test Substance Source	High	All Outcomes: The source of the test substance was Dow Chemical Company. Batch/lot number was not provided. The test material was analyzed prior to use and found to be 99.9% pure.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was reported to be 99.9% pure.
Domain 2: Test Desig	gn			
•	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Negative control group was included (filtered air).
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated.
Domain 3: Exposure	Characterization			
rr	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Storage and preparation conditions were not fully described, however, the test atmosphere was generated during each exposure period.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposure to test substance was consistent across study groups
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were reported and appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: There were deficiencies in number exposure groups and concentrations used. Rat teratology: only 2 concentrations studied, and the highest was lethal. Rabbit teratology: no effect was seen at highest concentration.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: A dynamic whole-body chamber was used. The number of air changes were not reported.
Domain 4: Test Anin	nals			
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Not all animal characteristics were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Husbandry conditions were adequately reported.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed per group were reported.

Study Citation: Rao, K.S., Murray, J.S., Deacon, M.M., John, J.A., Calhoun, L.L., Young, J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylene

dichloride. 5:P149-P166.

**Health** Mortality; Reproductive/Developmental;

**Outcome(s):** 

Reported Health Effect(s):

Mortality: Mortality; Reproductive/Developmental: Developmental Rat Study:Number of corpora lutea, number and position of live, dead and resorbed fetuses and fetal weight, length, sex, external alteration, skeletal alteration, and cleft palate. Developmental Rabbit Study: Number of corpora lutea, number

and position of live, dead and resorbed fetuses and fetal weight, length, sex, external alteration, skeletal alteration, and cleft palate. Reproductive Study in Rats: Fertility index, gestation days, sex ratio, neonatal body weight, gestation survival index, gross pathological examination of pups. Histology on

ovaries, uterus and testes.;

 Duration:
 Reproductive/Developmental Developmental

 Chemical:
 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5453539

Domain		Metric	Rating	Comments
Domain 5: Outcome	Assessment			
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methodologies were appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome assessment protocols were reported and consistently assessed across the study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: The sampling was adequate for outcomes evaluated.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were appropriate.
Domain 6: Confound	ling / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant and therefore respiratory rate should be reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	High	Mortality: Mortality was reported.; Reproductive/Developmental: Data were sufficiently reported

### **Overall Quality Determination**

### Medium

HERO ID: 5453539 Table: 2 of 4

Study Citation: Rao, K.S., Murray, J.S., Deacon, M.M., John, J.A., Calhoun, L.L., Young, J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylene

dichloride. 5:P149-P166. Nutritional/Metabolic

**Outcome(s):** 

**Reported Health** 

Body weight, food consumption

Effect(s):

Health

**Duration:**Reproductive/Developmental Developmental**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID.	3 133337			
Domain		Metric	Rating	Comments
Domain 1: Test Substa	ince			
	Metric 1:	Test Substance Identity	High	Test substance was identified as ethylene dichloride (1,2-dichlroethane).
	Metric 2:	Test Substance Source	High	The source of the test substance was Dow Chemical Company. Batch/lot number was not provided. The test material was analyzed prior to use and found to be 99.9% pure.
	Metric 3:	Test Substance Purity	High	The test substance was reported to be 99.9% pure.
Domain 2: Test Design	1			
	Metric 4:	Negative and Vehicle Controls	High	Negative control group was included (filtered air).
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure C	Characterization			
	Metric 7:	Preparation and Storage of Test Substance	Medium	Storage and preparation conditions were not fully described, however, the test atmosphere was generated during each exposure period.
	Metric 8:	Consistency of Exposure Administration	High	Exposure to test substance was consistent across study groups
	Metric 9:	Reporting of Doses/Concentrations	Low	Actual concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	There were deficiencies in number exposure groups and concentrations used. Rat teratology: only 2 concentrations studied, and the highest was lethal. Rabbit teratology: no effect was seen at highest concentration.
	Metric 12:	Exposure Route and Method	Medium	A dynamic whole-body chamber was used. The number of air changes were not reported.
Domain 4: Test Anima	als			
	Metric 13:	Test Animal Characteristics	Medium	Not all animal characteristics were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were adequately reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed per group were reported.
Domain 5: Outcome A	ssessment			
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodologies were appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment protocols were reported and consistently assessed across the study groups.
	Metric 18:	Sampling Adequacy	High	The sampling was adequate for outcomes evaluated.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.

HERO ID: 5453539 Table: 2 of 4

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Study Citation: Rao, K.S., Murray, J.S., Deacon, M.M., John, J.A., Calhoun, L.L., Young, J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylene

dichloride. 5:P149-P166. Nutritional/Metabolic

Outcome(s):

**Reported Health** 

Body weight, food consumption

**Effect(s):** 

Health

**Duration:**Reproductive/Developmental Developmental**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 5453539

Domain		Metric	Rating	Comments
	Metric 20:	Negative Control Response	High	The negative control responses were appropriate.
Domain 6: Confoundi	ing / Variable Cor	ntrol		
	Metric 21:	Confounding Variables in Test Design	Low	Test substance is a respiratory irritant and therefore respiratory rate should be reported.
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	Medium	Body weight data were not shown.

## **Overall Quality Determination**

## Medium

Study Citation:	Rao, K.S., M	Murray, J.S., Deacon, M.M., John, J.A., Calhot	un, L.L., Young	g, J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylene			
Health	dichloride.	5:P149-P166. deproductive/Developmental;					
Outcome(s):	Wiortanty, IX	reproductive, bevelopmental,					
Reported Health	Mortality: Mortality; Reproductive/Developmental: Developmental Rat Study:Number of corpora lutea, number and position of live, dead and resorbed						
Effect(s):	fetuses and	fetal weight, length, sex, external alteration, s	keletal alteratio	on, and cleft palate. Developmental Rabbit Study: Number of corpora lutea, number			
	•		~ ~	s, sex, external alteration, skeletal alteration, and cleft palate.Reproductive Study			
			al body weight	, gestation survival index, gross pathological examination of pups. Histology on			
Duration:	ovaries, uterus and testes.;						
Chemical:	Reproductive/Developmental Reproduction 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	5453539	130.11.01.11.12.21.01.10.20.01.11.10					
Domain		Metric	Rating	Comments			
Domain 1: Test Substan	ce						
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as ethylene dichloride (1,2-dichlroethane).			
	Metric 2:	Test Substance Source	High	All Outcomes: The source of the test substance was Dow Chemical Company. Batch/lot number was not provided. The test material was analyzed prior to use and found to be 99.9% pure.			
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was reported to be 99.9% pure.			
Domain 2: Test Design							
	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: A negative control group was included, but not all conditions were equal "Control animals were not placed in chamber because of lack of chamber space".			
	Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.			
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Study states animals were randomly allocated to groups.			
Domain 3: Exposure Ch	naroatarization						
Domain 3. Exposure Cir	Metric 7:	Preparation and Storage of Test	Medium	All Outcomes: Storage and preparation conditions were not fully described, however,			
	Wietite 7.	Substance	Wedium	the test atmosphere was generated during each exposure period.			
	Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure to test substance was consistent across study groups.			
	M-4 0.	Administration	T				
	Metric 9: Metric 10:	Reporting of Doses/Concentrations Exposure Frequency and Duration	Low	All Outcomes: Actual concentrations were not reported.  All Outcomes: Exposure frequency and duration were reported and appropriate.			
	Metric 11:	Number of Exposure Groups and	High Low	All Outcomes: There were deficiencies in number exposure groups and concentrations			
	Medic 11.	Dose/Concentration Spacing	Low	used, no effect was seen at highest concentration.			
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: A dynamic whole-body chamber was used. The number of air changes were not reported.			
D 4. Tt A : 1	_						
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	Medium	All Outcomes, Not all onimal characteristics were reported			
	Metric 13:	Adequacy and Consistency of Animal	High	All Outcomes: Not all animal characteristics were reported.  All Outcomes: Husbandry conditions were adequately reported.			
	14100110 17.	Husbandry Conditions	IIIgii	7111 Outcomes. Trasbandry conditions were adequatery reported.			
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals exposed per group were reported.			
Domain 5: Outcome As	sessment						
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methodologies were appropriate.			
		Contin	ued on next pa	NGP			
		Contin	ucu on next pa	···			

Mortality:	P149-P166.  Eproductive/Developmental;  Fortality; Reproductive/Developmental: Developmental weight, length, sex, external alteration, so of live, dead and resorbed fetuses and feta	velopmental Rat s skeletal alteration ll weight, length,	J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylen Study:Number of corpora lutea, number and position of live, dead and resorben, and cleft palate.Developmental Rabbit Study:Number of corpora lutea, number sex, external alteration, skeletal alteration, and cleft palate.Reproductive Studgestation survival index, gross pathological examination of pups. Histology of
Mortality; Remortality; Mortality; Mortality	productive/Developmental; cortality; Reproductive/Developmental: Developmental betal weight, length, sex, external alteration, of live, dead and resorbed fetuses and fetality index, gestation days, sex ratio, neonals and testes.; //Developmental Reproduction	skeletal alteration l weight, length,	n, and cleft palate.Developmental Rabbit Study:Number of corpora lutea, number sex, external alteration, skeletal alteration, and cleft palate.Reproductive Study
etuses and fe and position n Rats: Ferti ovaries, uteru Reproductive ,1-Dichloroo	etal weight, length, sex, external alteration, so flive, dead and resorbed fetuses and feta ility index, gestation days, sex ratio, neonals and testes.;  //Developmental Reproduction	skeletal alteration l weight, length,	n, and cleft palate.Developmental Rabbit Study:Number of corpora lutea, number sex, external alteration, skeletal alteration, and cleft palate.Reproductive Stud
etuses and fe and position n Rats: Ferti ovaries, uteru Reproductive ,1-Dichloroo	etal weight, length, sex, external alteration, so flive, dead and resorbed fetuses and feta ility index, gestation days, sex ratio, neonals and testes.;  //Developmental Reproduction	skeletal alteration l weight, length,	n, and cleft palate.Developmental Rabbit Study:Number of corpora lutea, number sex, external alteration, skeletal alteration, and cleft palate.Reproductive Study
and position in Rats: Fertiovaries, uteru Reproductive 1,1-Dichloroo	of live, dead and resorbed fetuses and feta ility index, gestation days, sex ratio, neonals and testes.; //Developmental Reproduction	l weight, length,	sex, external alteration, skeletal alteration, and cleft palate.Reproductive Stud
n Rats: Fertiovaries, uteru Reproductive 1,1-Dichloroo	ility index, gestation days, sex ratio, neona is and testes.; /Developmental Reproduction		
ovaries, uteru Reproductive ,1-Dichloro	s and testes.; /Developmental Reproduction	tal body weight,	gestation survival index, gross pathological examination of pups. Histology of
Reproductive ,1-Dichloro	/Developmental Reproduction		
,1-Dichloro			
1	ethane- Isomer: 1,2-Dichloroethane		
1433339			
	Metric	Rating	Comments
Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome assessment protocols were reported and consistently assessed across the study groups.
Metric 18:	Sampling Adequacy	High	All Outcomes: The sampling was adequate for outcomes evaluated.
Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were appropriate.
Variable Con	trol		
Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant and therefore respiratory rate should be reported.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: During the seventh week of the study, a syndrome similar to sialo- dacryoadenitis spread among both controland treated animals, subsiding after the eight week of the study.
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.
Metric 24:	Reporting of Data	High	Mortality: Mortality was reported.; Reproductive/Developmental: Data were sufficient reported.
\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	Metric 18: Metric 19: Metric 20: Variable Con Metric 21: Metric 22: Metric 23: Metric 24:	Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy Metric 19: Blinding of Assessors Metric 20: Negative Control Response  Variable Control Metric 21: Confounding Variables in Test Design and Procedures Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis	Metric 17: Consistency of Outcome Assessment High  Metric 18: Sampling Adequacy High  Metric 19: Blinding of Assessors N/A  Metric 20: Negative Control Response High  Variable Control  Metric 21: Confounding Variables in Test Design Low and Procedures  Metric 22: Health Outcomes Unrelated to Exposure  Metric 23: Data Presentation and Analysis High  Metric 24: Reporting of Data High

**Study Citation:** Rao, K.S., Murray, J.S., Deacon, M.M., John, J.A., Calhoun, L.L., Young, J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylene

dichloride. 5:P149-P166. Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic; Health

**Outcome(s):** 

**Reported Health** Renal/Kidney: Repro study: Kidney weight, histology; Hepatic/Liver: Repro study: Liver weight, histology; Nutritional/Metabolic: Body weight, food

Effect(s): consumption;

**Duration:** Reproductive/Developmental Reproduction 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane Chemical:

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified as ethylene dichloride (1,2-dichlroethane).
Metric 2:	Test Substance Source	High	All Outcomes: The source of the test substance was Dow Chemical Company. Batch/lot number was not provided. The test material was analyzed prior to use and found to be 99.9% pure.
Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was reported to be 99.9% pure.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: A negative control group was included, but not all conditions were equal "Control animals were not placed in chamber because of lack of chamber space".
Metric 5:	Positive Controls	N/A	All Outcomes: Positive control was not required in this study.
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Study states animals were randomly allocated to groups.
Domain 3: Exposure Characterizati	on		
Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Storage and preparation conditions were not fully described, however, the test atmosphere was generated during each exposure period.
Metric 8:	Consistency of Exposure	High	All Outcomes: Exposure to test substance was consistent across study groups.
Metric 9:	Administration Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were not reported.
Metric 10		High	All Outcomes: Exposure frequency and duration were reported and appropriate.
Metric 11		Low	All Outcomes: There were deficiencies in number exposure groups and concentrations
	Dose/Concentration Spacing		used, no effect was seen at highest concentration.
Metric 12		Medium	All Outcomes: A dynamic whole-body chamber was used. The number of air changes were not reported.
Domain 4: Test Animals			
Metric 13	: Test Animal Characteristics	Medium	All Outcomes: Not all animal characteristics were reported.
Metric 14	: Adequacy and Consistency of Animal	High	All Outcomes: Husbandry conditions were adequately reported.
	Husbandry Conditions		
Metric 15	: Number of Animals per Group	Medium	All Outcomes: The number of animals exposed per group were reported.
Domain 5: Outcome Assessment			
Metric 16	Outcome Assessment Methodology	High	Renal/Kidney: Outcome assessment methodologies were appropriate (organ weight and histology).; Hepatic/Liver: Outcome assessment methodologies were appropriate (organ weight and histology).; Nutritional/Metabolic: Outcome assessment methodologies were appropriate.

		continu	ıed from previ	ous page				
Study Citation:	Rao, K.S., Murray, J.S., Deacon, M.M., John, J.A., Calhoun, L.L., Young, J.T. (1980). Teratogenicity and reproduction studies in animals inhaling ethylene							
	dichloride. 5:P149-P166.							
Health	Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic;							
Outcome(s):								
Reported Health	Renal/Kidney: Repro study: Kidney weight, histology; Hepatic/Liver: Repro study: Liver weight, histology; Nutritional/Metabolic: Body weight, food							
Effect(s):	consumption	ı;						
<b>Duration:</b>	Reproductive	e/Developmental Reproduction						
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane						
HERO ID:	5453539							
Domain		Metric	Rating	Comments				
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome assessment protocols were reported and consistently assessed across the study groups.				
	Metric 18:	Sampling Adequacy	High	All Outcomes: The sampling was adequate for outcomes evaluated.				
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.				
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control responses were appropriate.				
Domain 6: Confound	ing / Variable Co	ntrol						
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Test substance is a respiratory irritant and therefore respiratory rate should be reported.				
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: During the seventh week of the study, a syndrome similar to sialo- dacryoadenitis spread among both controland treated animals, subsiding after the eighth week of the study.				
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.				
	Metric 24:	Reporting of Data	Low	Renal/Kidney: Organ weights were sufficiently reported, but histology was not.; Hepatic/Liver: Organ weights were sufficiently reported, but histology was not.; Nutritional/Metabolic: Body weight and food consumption data were not shown for all.				

## **Overall Quality Determination**

## Medium

**Study Citation:** 

WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Health

Neurological/Behavioral

**Outcome(s):** 

**Reported Health** FOB and motor activity in adult F1 offspring; behavioral clinical signs in F0 and F1 adults (changes in autonomic and central nervous systems, somatomotor **Effect(s):** 

activity and behavior); brain weights, macroscopic and microscopic analysis of nervous system tissues of F0 and F1 adults; brain histopathology for F1

weanlings

Reproductive/Developmental Extended 1-generation **Duration: Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substar	nce			
	Metric 1:	Test Substance Identity	High	The test substance was clearly identified as ethylene dichloride (CASRN 107-06-2). The form (colorless clear liquid) was reported.
	Metric 2:	Test Substance Source	High	The test substance was obtained from the sponsor (WIL Research). A certificate of analysis was included in the Appendix of the study report.
	Metric 3:	Test Substance Purity	High	The purity was 99.97%.
Domain 2: Test Design				
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	High	Negative control animals were allowed access to untreated reverse osmosis-purified deionized water.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	Parental F0 animals were randomly assigned into study groups using a computerized randomization procedure, based on a body weight stratification design. Animals were randomly selected for cohabitation, avoiding sibling matings. On PND4, litters were randomly (by computer randomization) culled to 10 pups per litter (5/sex). On PND21, offspring were again randomly selected to remain on the study.
Domain 3: Evnosura Cl	horoctarization			
Domain 3: Exposure Cl	haracterization Metric 7:	Preparation and Storage of Test Substance	High	The preparation and storage of the test substance and test solutions were described in detail, including the frequency of preparation. Stability testing was performed, and the treated drinking water formulations were mixed for at least 30 minutes. The test substance was soluble in water up to a concentration of 8 mg/mL.
Domain 3: Exposure C		-	High High	detail, including the frequency of preparation. Stability testing was performed, and the treated drinking water formulations were mixed for at least 30 minutes. The test
Domain 3: Exposure C	Metric 7:	Substance  Consistency of Exposure	-	detail, including the frequency of preparation. Stability testing was performed, and the treated drinking water formulations were mixed for at least 30 minutes. The test substance was soluble in water up to a concentration of 8 mg/mL.  Details of exposure administration were reported. Water was available to animals in all

Study Citation: WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Health Neurological/Behavioral

**Outcome(s):** 

Reported Health Effect(s):

FOB and motor activity in adult F1 offspring; behavioral clinical signs in F0 and F1 adults (changes in autonomic and central nervous systems, somatomotor activity and behavior); brain weights, macroscopic and microscopic analysis of nervous system tissues of F0 and F1 adults; brain histopathology for F1

weanlings

**Duration:**Reproductive/Developmental Extended 1-generation**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain	Metric	Rating	Comments
Metric	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups (3 treatment groups and one control) was consistent with OECD TG 443 recommendations. Dose selection and spacing rationale were provided (pg. 765/7697), and the spacing was sufficient for identifying NOAEL and LOAEL values.
Metric	2: Exposure Route and Method	High	The exposure route (via drinking water) was appropriate for the test substance. The test substance is considered to be a volatile organic compound; however, except for a few isolated occurrences, analytical measurements of the test substance in the test solutions remained within 90-110% of the target.
Domain 4: Test Animals			
Metric	3: Test Animal Characteristics	High	The test animal species, strain, sex, age, starting body weights, and source were reported, and justification for their use was provided in the study. Parity was not specified, but animals were reported to be "sexually mature."
Metric	4: Adequacy and Consistency of Animal Husbandry Conditions	High	A detailed description of all animal husbandry conditions was provided. Conditions were consistent across groups.
Metric		Medium	The number of animals per group was reported and adhered to OECD TG 443 guide- lines, which specifies using enough mating pairs to obtain at least 20 litters.
Domain 5: Outcome Assessment			
Metric	6: Outcome Assessment Methodology	High	The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.
Metric	7: Consistency of Outcome Assessment	High	Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.
Metric	8: Sampling Adequacy	High	Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.
Metric	9: Blinding of Assessors	High	Blinding is required for some neurological endpoints. FOB and targeted histopathological morphometric analysis was performed blind.
Metric	20: Negative Control Response	High	The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.

Domain 6: Confounding / Variable Control

•••	continued from previous page

Study Citation: WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Health Neurological/Behavioral

**Outcome(s):** 

**Reported Health** FOB and motor activity in adult F1 offspring; behavioral clinical signs in F0 and F1 adults (changes in autonomic and central nervous systems, somatomotor activity and behavior); brain weights, macroscopic and microscopic analysis of nervous system tissues of F0 and F1 adults; brain histopathology for F1

weanlings

**Duration:** Reproductive/Developmental Extended 1-generation **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain		Metric	Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	The study authors did note that concentration-dependent reductions in water intake throughout the study period were likely due to issues with palatability. This resulted in exposure levels that were generally below the target. Water intake was reduced by >20% in the mid-and high-dose groups, and there were corresponding reductions in body weights. The authors noted that many of the effects observed (decreased body weights, organ weight changes etc.,) stemmed from the reduced water intake and likely dehydration. Several other minor protocol deviations or errors were detailed; none of these was considered to have a significant impact on the study results.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	There were some health outcomes unrelated to exposure. Two high-dose F0 males died. The cause of death in one male was undetermined, the other male developed malignant lymphoma. Two high-dose F0 females also died, one had a fractured bone, and another exhibited signs of an acute infarction of multiple organs. None of these deaths was considered to be related to treatment. In F1 animals, one low-dose male was sacrificed in extremis (no cause determined). One control and one high-dose F1 female died, and these deaths were considered to be incidental. None of these deaths is suggestive of significant attrition and is not expected to have a significant impact on the study results.
	Metric 23:	Data Presentation and Analysis	High	Statistical methodology were described in detail and were appropriate for the data sets. Additionally, all data were provided allowing for an independent analysis.
	Metric 24:	Reporting of Data	High	Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.)

### **Overall Quality Determination**

### Uninformative

**Study Citation:** 

WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Health

Clinical signs (Clinical Signs)

**Outcome(s):** 

**Reported Health** Clinical signs (non-behavioral) (e.g., changes in the appearance of skin and fur, eyes, mucous membranes, respiratory, and circulatory system; for example:

Effect(s): dried material around eyes and nose, hair loss, decreased defecation, etc.,) of F0 and F1 adults

**Duration:** Reproductive/Developmental Extended 1-generation **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID.	7310770			
Domain		Metric	Rating	Comments
Domain 1: Test Substan	ce			
	Metric 1:	Test Substance Identity	High	The test substance was clearly identified as ethylene dichloride (CASRN 107-06-2). The form (colorless clear liquid) was reported.
	Metric 2:	Test Substance Source	High	The test substance was obtained from the sponsor (WIL Research). A certificate of analysis was included in the Appendix of the study report.
	Metric 3:	Test Substance Purity	High	The purity was 99.97%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative control animals were allowed access to untreated reverse osmosis-purified deionized water.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Medium	Parental F0 animals were randomly assigned into study groups using a computerized randomization procedure, based on a body weight stratification design. Animals were randomly selected for cohabitation, avoiding sibling matings. On PND4, litters were randomly (by computer randomization) culled to 10 pups per litter (5/sex). On PND21, offspring were again randomly selected to remain on the study.
Domain 3: Exposure Ch	naracterization			
2011an	Metric 7:	Preparation and Storage of Test Substance	High	The preparation and storage of the test substance and test solutions were described in detail, including the frequency of preparation. Stability testing was performed, and the treated drinking water formulations were mixed for at least 30 minutes. The test substance was soluble in water up to a concentration of 8 mg/mL.
	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported. Water was available to animals in all groups ad libitum. There was no evidence of inconsistent exposures across groups.
	Metric 9:	Reporting of Doses/Concentrations	High	The study authors reported both target doses and mean calculated doses based on water concentration, water intake and body weight data (pg. 35, 105,and 126/7697). An overall time-weighted average dose for each sex and generation was not determined; for example, separate calculated doses were determined for F0 males during pre-mating and after mating, and for F0 females, separate doses prior to mating, and during gestation, and lactation. However, sufficient information is available to independently determine an overall TWA dose if desired, and water intake and body weight data were provided. The study also specified how dose adjustments were conducted (pg. 766/7697).
	Metric 10:	Exposure Frequency and Duration	High	The exposure duration and frequency adhered to the OECD TG 443 guideline.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups (3 treatment groups and one control) was consistent with OECD TG 443 recommendations. Dose selection and spacing rationale were provided (pg. 765/7697), and the spacing was sufficient for identifying NOAEL and LOAEL values.
		Cont	inued on next page	

**Study Citation:** WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats. Clinical signs (Clinical Signs)

Health

**Outcome(s):** 

Reported Health

Clinical signs (non-behavioral) (e.g., changes in the appearance of skin and fur, eyes, mucous membranes, respiratory, and circulatory system; for example:

dried material around eyes and nose, hair loss, decreased defecation, etc.,) of F0 and F1 adults

Effect(s): **Duration:** Chemical:

Reproductive/Developmental Extended 1-generation 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HEDO ID.

7310776			
	Metric	Rating	Comments
Metric 12:	Exposure Route and Method	High	The exposure route (via drinking water) was appropriate for the test substance. The test substance is considered to be a volatile organic compound; however, except for a few isolated occurrences, analytical measurements of the test substance in the test solutions remained within 90-110% of the target.
als			
Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, starting body weights, and source were reported, and justification for their use was provided in the study. Parity was not specified but animals were reported to be "sexually mature."
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	A detailed description of all animal husbandry conditions was provided. Conditions were consistent across groups.
Metric 15:	Number of Animals per Group	Medium	The number of animals per group was reported and adhered to OECD TG 443 guide- lines, which specifies using enough mating pairs to obtain at least 20 litters.
Assessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.
Metric 17:	Consistency of Outcome Assessment	High	Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.
Metric 18:	Sampling Adequacy	High	Sampling was clearly noted in all data tables and was adequate for the outcomes of interest.
Metric 19:	Blinding of Assessors	Low	The study did not specify whether the clinical observations were conducted in a blinded manner and this outcome is somewhat subjective in nature
Metric 20:	Negative Control Response	High	The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.
ng / Variable Co	ntrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	The study authors did note that concentration-dependent reductions in water intake throughout the study period were likely due to issues with palatability. This resulted in exposure levels that were generally below the target. Water intake was reduced by >20% in the mid-and high-dose groups, and there were corresponding reductions in body weights. The authors noted that many of the effects observed (decreased body weights, organ weight changes etc) stemmed from the reduced water intake and likely dehydration. Several other minor protocol deviations or errors were detailed; none of these was considered to have a significant impact on the study results.
	Metric 12:  als Metric 13: Metric 14: Metric 15:  Assessment Metric 16: Metric 17: Metric 18: Metric 19: Metric 20:	Metric 12: Exposure Route and Method  als  Metric 13: Test Animal Characteristics  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group  Assessment  Metric 16: Outcome Assessment Methodology  Metric 17: Consistency of Outcome Assessment  Metric 18: Sampling Adequacy  Metric 19: Blinding of Assessors  Metric 20: Negative Control Response  ng / Variable Control  Metric 21: Confounding Variables in Test Design	Metric 12: Exposure Route and Method High  Als  Metric 13: Test Animal Characteristics High  Metric 14: Adequacy and Consistency of Animal Husbandry Conditions  Metric 15: Number of Animals per Group Medium  Assessment  Metric 16: Outcome Assessment Methodology High  Metric 17: Consistency of Outcome Assessment High  Metric 18: Sampling Adequacy High  Metric 19: Blinding of Assessors Low  Metric 20: Negative Control Response High  mg / Variable Control  Metric 21: Confounding Variables in Test Design Uninformative

**Study Citation:** WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Health

Clinical signs (Clinical Signs)

**Outcome(s):** 

Clinical signs (non-behavioral) (e.g., changes in the appearance of skin and fur, eyes, mucous membranes, respiratory, and circulatory system; for example: Reported Health

Effect(s): dried material around eyes and nose, hair loss, decreased defecation, etc.,) of F0 and F1 adults

**Duration:** Reproductive/Developmental Extended 1-generation Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to	High	There were some health outcomes unrelated to exposure. Two high-dose F0 males died.
		Exposure		The cause of death in one male was undetermined, the other male developed malignant
		•		lymphoma. Two high-dose F0 females also died, one had a fractured bone, and another
				exhibited signs of an acute infarction of multiple organs. None of these deaths was con-
				sidered to be related to treatment. In F1 animals, one low-dose male was sacrificed in
				extremis (no cause determined). One control and one high-dose F1 female died, and
				these deaths were considered to be incidental. None of these deaths is suggestive of
				significant attrition and is not expected to have a significant impact on the study results.
	Metric 23:	Data Presentation and Analysis	High	Statistical methodology were described in detail and were appropriate for the data sets.
		•	_	Additionally, all data were provided allowing for an independent analysis.
	Metric 24:	Reporting of Data	High	Summary tables reporting incidences and sample size and individual animal data were provided.

### **Overall Quality Determination**

### Uninformative

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

**Duration:** Reproductive/Developmental Extended 1-generation

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

	Metric	Rating	Comments
nce			
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was clearly identified as ethylene dichloride (CASRN 107-06-2). The form (colorless clear liquid) was reported.
Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from the sponsor (WIL Research). A certificate of analysis was included in the Appendix of the study report.
Metric 3:	Test Substance Purity	High	All Outcomes: The purity was 99.97%.
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Negative control animals were allowed access to untreated reverse osmosis-purified deionized water.
Metric 5:	Positive Controls	N/A	All Outcomes: Positive controls are not required for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Parental F0 animals were randomly assigned into study groups using a computerized randomization procedure, based on a body weight stratification design. Animals were randomly selected for cohabitation, avoiding sibling matings. On PND4, litters were randomly (by computer randomization) culled to 10 pups per litter (5/sex). On PND21, offspring were again randomly selected to remain on the study.
haracterization			
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The preparation and storage of the test substance and test solutions were described in detail, including the frequency of preparation. Stability testing was performed, and the treated drinking water formulations were mixed for at least 30 minutes. The test substance was soluble in water up to a concentration of 8 mg/mL.
	Metric 1: Metric 2: Metric 3:  Metric 4: Metric 5: Metric 6:	Metric 1: Test Substance Identity  Metric 2: Test Substance Source  Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls  Metric 5: Positive Controls  Metric 6: Randomized Allocation of Animals  haracterization  Metric 7: Preparation and Storage of Test	Metric 1: Test Substance Identity High  Metric 2: Test Substance Source High  Metric 3: Test Substance Purity High  Metric 4: Negative and Vehicle Controls High  Metric 5: Positive Controls N/A  Metric 6: Randomized Allocation of Animals Medium  haracterization  Metric 7: Preparation and Storage of Test High

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Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

Duration: Reproductive/Developmental Extended 1-generation
Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain	Metric	Rating	Comments
Metric	8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported. Water was available to animals in all groups ad libitum. There was no evidence of inconsistent exposures across groups.

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

**Duration:** Reproductive/Developmental Extended 1-generation

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Chemical:

Domain Metric Rating Comments

Metric 9: Reporting of Doses/Concentrations High Mortality: The study authors reported both target doses and mean calculated doses based

on water concentration, water intake and body weight data (pg. 35/7697). An overall time-weighted average dose for each sex and generation was not determined; for example, separate calculated doses were determined for F0 males during pre-mating and after mating, and for F0 females, separate doses prior to mating, and during gestation, and lactation. However, sufficient information is available to independently determine an overall TWA dose if desired, and water intake and body weight data were provided. The study also specified how dose adjustments were conducted (pg. 766/7697).; Endocrine (Endocrine): The study authors reported both target doses and mean calculated doses based on water concentration, water intake and body weight data (pg. 35, 105, and 126/7697). An overall time-weighted average dose for each sex and generation was not determined; for example, separate calculated doses were determined for F0 males during pre-mating and after mating, and for F0 females, separate doses prior to mating, and during gestation, and lactation. However, sufficient information is available to independently determine an overall TWA dose if desired, and water intake and body weight data were provided. The study also specified how dose adjustments were conducted (pg. 766/7697).; Nutritional/Metabolic: The study authors reported both target doses and mean calculated doses based on water concentration, water intake and body weight data (pg. 35, 105, and 126/7697). An overall time-weighted average dose for each sex and generation was not determined; for example, separate calculated doses were determined for F0 males during pre-mating and after mating, and for F0 females, separate doses prior to mating, and during gestation, and lactation. However, sufficient information is available to independently determine an overall TWA dose if desired, and water intake and body weight data were provided. The study also specified how dose adjustments were conducted (pg. 766/7697).; Immune/Hematological: The study authors reported both target doses and mean calculated doses based on water concentration, water intake and body weight data (pg. 35, 105, and 126/7697). An overall time-weighted average dose for each sex and generation was not determined; for example, separate calculated doses were determined for F0 males during pre-mating and after mating, and for F0 females, separate doses prior to mating, and during gestation, and lactation. However, sufficient information is available to independently determine an overall TWA

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

**Duration:** Chemical:

Reproductive/Developmental Extended 1-generation 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure duration and frequency adhered to the OECD TG 443 guideline.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups (3 treatment groups and one control) was consistent with OECD TG 443 recommendations. Dose selection and spacing rationale were provided (pg. 765/7697), and the spacing was sufficient for identifying NOAEL and LOAEL values.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The exposure route (via drinking water) was appropriate for the test substance. The test substance is considered to be a volatile organic compound; however, except for a few isolated occurrences, analytical measurements of the test substance in the test solutions remained within 90-110% of the target.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, age, starting body weights, and source were reported, and justification for their use was provided in the study. Parity was not specified, but animals were reported to be "sexually mature."
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: A detailed description of all animal husbandry conditions was provided. Conditions were consistent across groups.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and adhered to OECD TG 443 guidelines, which specifies using enough mating pairs to obtain at least 20 litters.

Domain 5: Outcome Assessment

**Study Citation:** Health Outcome(s): Reported Health Effect(s):

WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; Thyroid: Thyroid hormones (T4, TSH), organ histopathology of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts); Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults; Musculoskeletal: Detailed histopathology of musculoskeletal-related tissues of F0 and F1 adults;

**Duration:** Reproductive/Developmental Extended 1-generation Chemical:

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

> Domain Metric Rating Comments

> > Metric 16: Outcome Assessment Methodology High Mortality: The outcome methodology was reported and appropriate for the purposes of

the study. Animals were observed daily.; Endocrine (Endocrine): The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Nutritional/Metabolic: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Immune/Hematological: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Hepatic/Liver: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Renal/Kidney: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Thyroid: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Lung/Respiratory: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Gastrointestinal: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Ocular/Sensory: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Reproductive/Developmental: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Cardiovascular: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.; Musculoskeletal: The outcome methodology was reported and was appropriate and sensitive for the outcomes of interest.

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-testinal, Oppler/Consorry, Percentus (Conditional States of Conditional Stat

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

**Duration:** Chemical:

Reproductive/Developmental Extended 1-generation 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain Metric Rating Comments

Metric 17: Consistency of Outcome Assessment High

Mortality: The time of day of the outcome assessment was not specified, but all animals were observed daily for signs of mortality. The absence of a specified time is not expected to have an impact on the study results.; Endocrine (Endocrine): Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Nutritional/Metabolic: Specific details on the timing of body weight measurements, food consumption and water intake were reported in the methods and the outcomes were consistently assessed across all groups.; Immune/Hematological: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Hepatic/Liver: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Renal/Kidney: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Thyroid: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Lung/Respiratory: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Gastrointestinal: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Ocular/Sensory: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Reproductive/Developmental: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Cardiovascular: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.; Musculoskeletal: Information on the timing of the outcome assessment for each generation was provided in detail, and the outcomes were assessed consistently across groups.

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues

of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes,

necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of FO

and F1 adults; Musculoskeletal: Detailed histopathology of musculoskeletal-related tissues of F0 and F1 adults; Reproductive/Developmental Extended 1-generation

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

**Duration:** 

Domain Metric Rating Comments

Metric 18: Sampling Adequacy High

Mortality: Sampling for this outcome included all animals.; Endocrine (Endocrine): Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Nutritional/Metabolic: Sampling for this outcome included all animals.; Immune/Hematological: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Hepatic/Liver: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Renal/Kidney: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Thyroid: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Lung/Respiratory: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Gastrointestinal: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Ocular/Sensory: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Reproductive/Developmental: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Cardiovascular: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.; Musculoskeletal: Sampling was clearly noted in all data tables and was adequate for the outcomes of interest. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose

subjective in nature.; Cardiovascular: Blinding is not required because the outcome(s) are not subjective in nature.; Musculoskeletal: Blinding is not required because the out-

come(s) are not subjective in nature.

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Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

**Duration:** Chemical:

Reproductive/Developmental Extended 1-generation 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain Metric Rating Comments Metric 19: Blinding of Assessors N/A Mortality: Blinding is not required for this outcome of interest because the endpoint(s) were not subjective in nature.; Endocrine (Endocrine): Blinding is not required because the outcome(s) are not subjective in nature.; Nutritional/Metabolic: Blinding is not required for this outcome of interest because the endpoint(s) were not subjective in nature.; Immune/Hematological: Blinding is not required because the outcome(s) are not subjective in nature.; Hepatic/Liver: Blinding is not required because the outcome(s) are not subjective in nature.; Renal/Kidney: Blinding is not required because the outcome(s) are not subjective in nature.; Thyroid: Blinding is not required because the outcome(s) are not subjective in nature.; Lung/Respiratory: Blinding is not required because the outcome(s) are not subjective in nature.; Gastrointestinal: Blinding is not required because the outcome(s) are not subjective in nature.; Ocular/Sensory: Blinding is not required because the outcome(s) are not subjective in nature.; Reproductive/Developmental: Blinding was used for appropriate outcomes (e.g., FOB), but blinding is not required for any of the reproductive/developmental outcomes evaluated because they were not

### ... continued from previous page

**Study Citation:** Health Outcome(s): Effect(s):

WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Reported Health

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; Thyroid: Thyroid hormones (T4, TSH), organ histopathology of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts); Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults; Musculoskeletal: Detailed histopathology of musculoskeletal-related tissues of F0 and F1 adults;

**Duration:** Chemical:

Reproductive/Developmental Extended 1-generation

**HERO ID:** 

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

7310776

Domain Metric Rating Metric 20: Negative Control Response High

Mortality: The biological responses of the negative controls were appropriate. No control animals died.; Endocrine (Endocrine): The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Nutritional/Metabolic: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Immune/Hematological: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Hepatic/Liver: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Renal/Kidney: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Thyroid: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Lung/Respiratory: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Gastrointestinal: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Ocular/Sensory: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Reproductive/Developmental: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Cardiovascular: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.; Musculoskeletal: The biological responses of the negative controls were reported and were appropriate. The study also provided historical control data for most endpoints.

Comments

### ... continued from previous page

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

**Duration:** 

Reproductive/Developmental Extended 1-generation

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain Metric Rating Comments

Domain 6: Confounding / Variable Control

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

**Duration:** Reproductive/Developmental Extended 1-generation

**HERO ID:** 7310776

Chemical:

Domain Metric Rating Comments

Metric 21: Confounding Variables in Test Design and Procedures

1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Uninformative

Mortality: The study authors did note that concentration-dependent reductions in water intake throughout the study period were likely due to issues with palatability. This resulted in exposure levels that were generally below the target. Water intake was reduced by >20% in the mid-and high-dose groups, and there were corresponding reductions in body weights. The authors noted that many of the effects observed (decreased body weights, organ weight changes etc.,) stemmed from the reduced water intake and likely dehydration. Several other minor protocol deviations or errors were detailed; none of these was considered to have a significant impact on the study results.; Endocrine (Endocrine): The study authors did note that concentration-dependent reductions in water intake throughout the study period were likely due to issues with palatability. This resulted in exposure levels that were generally below the target. Water intake was reduced by >20% in the mid-and high-dose groups, and there were corresponding reductions in body weights. The authors noted that many of the effects observed (decreased body weights, organ weight changes etc.,) stemmed from the reduced water intake and likely dehydration. Several other minor protocol deviations or errors were detailed; none of these was considered to have a significant impact on the study results.; Nutritional/Metabolic: The study authors did note that concentration-dependent reductions in water intake throughout the study period were likely due to issues with palatability. This resulted in exposure levels that were generally below the target. Water intake was reduced by >20% in the mid-and high-dose groups, and there were corresponding reductions in body weights. The authors noted that many of the effects observed (decreased body weights, organ weight changes etc.,) stemmed from the reduced water intake and likely dehydration. Several other minor protocol deviations or errors were detailed; none of these was considered to have a significant impact on the study results.; Immune/Hematological: The study authors did note that concentration-dependent reductions in water intake throughout the study period were likely due to issues with palatability. This resulted in exposure levels that were generally below the target. Water intake was reduced by >20% in the mid-and high-dose groups, and there were corresponding reductions in body weights. The authors noted that many of the effects observed (decreased body weights, organ weight changes etc.,) stemmed from the reduced water intake and likely dehydration. Several other minor protocol deviations or errors were

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; Thyroid hormones (T4, TSH), organ histopathology of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinatio

**Duration:** Chemical:

Reproductive/Developmental Extended 1-generation 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: There were some health outcomes unrelated to exposure. Two high-dose F0 males died. The cause of death in one male was undetermined, the other male developed malignant lymphoma. Two high-dose F0 females also died, one had a fractured bone, and another exhibited signs of an acute infarction of multiple organs. None of these deaths was considered to be related to treatment. In F1 animals, one low-dose male was sacrificed in extremis (no cause determined). One control and one high-dose F1 female died, and these deaths were considered to be incidental. None of these deaths is suggestive of significant attrition and is not expected to have a significant impact on the study results.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methodology were described in detail and were appropriate for the data sets. Additionally, all data were provided allowing for an independent analysis.

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0 and F1 adults

Duration: Chemical:

Reproductive/Developmental Extended 1-generation 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

Domain Metric Rating Comments

Metric 24: Reporting of Data High

Mortality: Mortality data were adequately reported. The number of animals that died, the causes and the times of death were specified.; Endocrine (Endocrine): Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.; Nutritional/Metabolic: Summary tables and individual animal data were provided. Means and both SD and SEM were reported along with the sample size (n); Immune/Hematological: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.; Hepatic/Liver: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.; Renal/Kidney: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.; Thyroid: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.; Lung/Respiratory: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.; Gastrointestinal: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.; Ocular/Sensory: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.; Reproductive/Developmental: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted.); Cardiovascular: Summary tables and individual animal data were provided. Means and both SD and SEM were reported when relevant along with the sample size (n). Other data were presented as incidences, and severity was noted. Musculoskeletal: Summary

Study Citation: Health Outcome(s): Reported Health Effect(s): WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.

Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastroin-

testinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;

Mortality: Mortality of F0 and F1 adults; Endocrine (Endocrine): Pituitary organ weights, macroscopic and microscopic examination of endocrine tissues (pituitary, pancreas, adrenals) of F0 and F1 adults; Nutritional/Metabolic: Body weights and body weight gain and food and water consumption of F0 and F1 adults; Immune/Hematological: Hematology and coagulation in F0 and F1 adults, organ weights (thymus and spleen), macroscopic and microscopic examinations (thymus, spleen, lymph nodes) of F0 and F1 adults; spleen and thymus histopathology for F1 weanlings; Hepatic/Liver: Related serum chemistry (albumin, globulin, A/G, total protein, bilirubin, ALP, AST, ALT, GGT, glucose, cholesterol, triglycerides), organ weights, gross and microscopic examinations of F0 and F1 adults; Renal/Kidney: Related serum chemistry (BUN, creatinine, electrolytes), urinalysis (specific gravity, pH, urobilinogen, total volume), organ weights, gross and microscopic examinations of F0 and F1 adults; thyroid histopathology for F1 weanlings; Lung/Respiratory: Macroscopic and microscopic examinations of all respiratory related tissues of F0 and F1 adults; Gastrointestinal: Necropsy, and detailed histopathology of all gastrointestinal-related tissues of F0 and F1 adults; Ocular/Sensory: Histopathology of eyes and related tissues (e.g., hardarian glands) of F0 and F1 adults; Reproductive/Developmental: Reproductive (F0: estrous cyclicity, reproductive performance, gestation length, sperm parameters, reproductive organ weights and histopathology, ovarian primordial follicle and corpora lutea counts);Developmental (F1: Litter and pup viability, postnatal survival, clinical observations, anogenital distance, body weights, weight changes, necropsy, organ weights hormones, areola/nipple retention, balanopreputial separation, vaginal patency, time of first estrous, FOB, motor activity, organ histopathology); Cardiovascular: Heart organ weights, Macroscopic and microscopic examinations of the heart and cardiovascular-related tissues of F0

and F1 adults; Musculoskeletal: Detailed histopathology of musculoskeletal-related tissues of F0 and F1 adults; Reproductive/Developmental Extended 1-generation

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 7310776

**Duration:** 

Domain Metric Rating Comments

### **Overall Quality Determination**

Study Citation: Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-

202.

Health Reproductive/Developmental

**Outcome(s):** 

**Reported Health** Pregnancy rates of exposed females, pregnancy rates of females mated with exposed males, preimplantation loss, post-implantation loss, pup survival, pup

**Effect(s):** weight and growth, structural teratology examinations, pup agitation in open space experiments

**Duration:**Reproductive/Developmental Rats- 5 weeks**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments
Domain 1: Test Substa	ance			
	Metric 1:	Test Substance Identity	High	Test substance was identified 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	The source of the test substance was Beijing Chemical Plant Two. Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	The purity of test substance was reported as 98.5%.
Domain 2: Test Design	n			
C	Metric 4:	Negative and Vehicle Controls	Low	It is not clear if the animals were untreated or sham exposed.
	Metric 5:	Positive Controls	N/A	A positive control was not needed.
	Metric 6:	Randomized Allocation of Animals	Low	The study does not report how animals were allocated.
Domain 3: Exposure (	Characterization			
r	Metric 7:	Preparation and Storage of Test	Low	The preparation and storage of test substance were not reported.
	Metric 8:	Substance Consistency of Exposure	Low	Details on exposure administration are insufficiently reported.
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Actual concentrations were reported, however the analytical method used to make these measurements was not reported.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency was appropriate (6 hrs/day).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Minor limitations with the number of exposure groups (a full range or responses were not obtained).
	Metric 12:	Exposure Route and Method	Uninformative	There is no description of the inhalation chamber.
Domain 4: Test Anima	als			
20114111 11 1000 1 1111111	Metric 13:	Test Animal Characteristics	Medium	Starting body weights and age were not reported.
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.
		Husbandry Conditions		,
	Metric 15:	Number of Animals per Group	Low	The number of animals/group was not reported.
Domain 5: Outcome A	Assessment			
	Metric 16:	Outcome Assessment Methodology	Low	Outcome methodology were not clearly reported.
	Metric 17:	Consistency of Outcome Assessment	Low	There were no details regarding the execution of the study protocol.
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.
		Col	ntinued on next page .	

Study Citation: Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-

202.

**Health** Reproductive/Developmental

**Outcome(s):** 

**Reported Health** Pregnancy rates of exposed females, pregnancy rates of females mated with exposed males, preimplantation loss, post-implantation loss, pup survival, pup

Effect(s): weight and growth, structural teratology examinations, pup agitation in open space experiments

**Duration:** Reproductive/Developmental Rats- 5 weeks **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200708

Domain		Metric	Rating	Comments	
	Metric 20:	Negative Control Response	Low	The negative control responses were not reported.	
Domain 6: Confoun	nding / Variable Cor	ntrol			
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Respiratory rates were not reported and are needed since the test substance is a respiratory irritant.	
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.	
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed but not described adequately.	
	Metric 24:	Reporting of Data	Low	Data were not reported adequately.	

### **Overall Quality Determination**

HERO ID: 200708 Table: 2 of 5

Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-**Study Citation:** 

Health Nutritional/Metabolic; Hepatic/Liver; Immune/Hematological; Renal/Kidney;

Outcome(s):

Reported Health Nutritional/Metabolic: Body weight of pregnant rats (5 weeks); Hepatic/Liver: Serum ALT (GPT) and AST (GOT) for pregnant rat (5 weeks); Im-

Effect(s): mune/Hematological: Hematology for pregnant rats (5 week); Renal/Kidney: Urinary protein in pregnant rats;

**Duration:** Reproductive/Developmental Rats- 5 weeks Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

etric 1: etric 2: etric 3: etric 4: etric 5: etric 6:	Metric  Test Substance Identity Test Substance Source  Test Substance Purity  Negative and Vehicle Controls Positive Controls	Rating High Low High Low	Comments  All Outcomes: Test substance was identified 1,2-dichloroethane.  All Outcomes: The source of the test substance was Beijing Chemical Plant Two.  Batch/lot number was not provided.  All Outcomes: The purity of test substance was reported as 98.5%.  All Outcomes: It is not clear if the animals were untreated or sham exposed.
etric 2: etric 3: etric 4: etric 5:	Test Substance Source  Test Substance Purity  Negative and Vehicle Controls Positive Controls	Low High Low	All Outcomes: The source of the test substance was Beijing Chemical Plant Two. Batch/lot number was not provided. All Outcomes: The purity of test substance was reported as 98.5%.
etric 2: etric 3: etric 4: etric 5:	Test Substance Source  Test Substance Purity  Negative and Vehicle Controls Positive Controls	Low High Low	All Outcomes: The source of the test substance was Beijing Chemical Plant Two. Batch/lot number was not provided. All Outcomes: The purity of test substance was reported as 98.5%.
etric 3: etric 4: etric 5:	Test Substance Purity  Negative and Vehicle Controls Positive Controls	High	Batch/lot number was not provided. All Outcomes: The purity of test substance was reported as 98.5%.
etric 4:	Negative and Vehicle Controls Positive Controls	Low	
etric 5:	Positive Controls		All Outcomes: It is not clear if the enimals were untreated or share evened.
etric 5:	Positive Controls		All Outgomes. It is not clear if the enimals were untracted or show expected
			An Outcomes. It is not clear if the animals were untreated or snam exposed.
etric 6:	D 1 ' 1 A 11 ' C A ' 1	N/A	All Outcomes: A positive control was not needed.
	Randomized Allocation of Animals	Low	All Outcomes: The study does not report how animals were allocated.
terization			
etric 7:	Preparation and Storage of Test	Low	All Outcomes: The preparation and storage of test substance were not reported.
etric 8:	Consistency of Exposure	Low	All Outcomes: Details on exposure administration are insufficiently reported.
etric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were reported, however the analytical method used to make these measurements was not reported.
etric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency was appropriate (6 hrs/day).
etric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Minor limitations with the number of exposure groups (a full range or responses were not obtained).
etric 12:	Exposure Route and Method	Uninformative	All Outcomes: There is no description of the inhalation chamber.
etric 13:	Test Animal Characteristics	Medium	All Outcomes: Starting body weights and age were not reported.
etric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not reported.
etric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals/group was not reported.
nent			
etric 16:	Outcome Assessment Methodology	Medium	Nutritional/Metabolic: Details on methodology were not reported.; Hep- atic/Liver: Serum ALT and AST were evaluated. No histology or liver weight.; Im- mune/Hematological: Details on which parameters assessed were not reported.; Re- nal/Kidney: Only urinary protein was evaluated.
etric 17:	Consistency of Outcome Assessment	Low	All Outcomes: There were no details regarding the execution of the study protocol.
etric 18:	Sampling Adequacy	Low	All Outcomes: Details regarding sampling of outcomes were not reported.
et e	tric 8: tric 9: tric 10: tric 11: tric 12: tric 13: tric 14: tric 15: ent tric 16:	tric 7: Preparation and Storage of Test Substance Consistency of Exposure Administration Reporting of Doses/Concentrations  tric 10: Exposure Frequency and Duration Number of Exposure Groups and Dose/Concentration Spacing Exposure Route and Method  tric 12: Test Animal Characteristics tric 14: Adequacy and Consistency of Animal Husbandry Conditions tric 15: Number of Animals per Group  ent tric 16: Outcome Assessment Methodology  tric 17: Consistency of Outcome Assessment tric 18: Sampling Adequacy	tric 7: Preparation and Storage of Test Substance tric 8: Consistency of Exposure Administration Reporting of Doses/Concentrations Low tric 10: Exposure Frequency and Duration High tric 11: Number of Exposure Groups and Dose/Concentration Spacing tric 12: Exposure Route and Method Uninformative  tric 13: Test Animal Characteristics Medium Husbandry Conditions tric 14: Adequacy and Consistency of Animal Husbandry Conditions tric 15: Number of Animals per Group Low  ent tric 16: Outcome Assessment Methodology Medium  tric 17: Consistency of Outcome Assessment Low

HERO ID: 200708 Table: 2 of 5

#### ... continued from previous page

**Study Citation:** Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-

Nutritional/Metabolic; Hepatic/Liver; Immune/Hematological; Renal/Kidney; Health

**Outcome(s):** 

Reported Health Nutritional/Metabolic: Body weight of pregnant rats (5 weeks); Hepatic/Liver: Serum ALT (GPT) and AST (GOT) for pregnant rat (5 weeks); Im-

Effect(s): mune/Hematological: Hematology for pregnant rats (5 week); Renal/Kidney: Urinary protein in pregnant rats;

**Duration:** Reproductive/Developmental Rats- 5 weeks Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200708

Domain		Metric	Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not needed to assess outcomes.
	Metric 20:	Negative Control Response	Low	All Outcomes: The negative control responses were not reported.
Domain 6: Confound	ding / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Respiratory rates were not reported and are needed since the test substance is a respiratory irritant.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Low	All Outcomes: Statistical analysis was performed but not described adequately.
	Metric 24:	Reporting of Data	Medium	Nutritional/Metabolic: Effects on maternal body weights were indicated as negative in the text.; Hepatic/Liver: Indicated as negative in the text.; Immune/Hematological: Hematological outcomes were indicated as negative in the text.; Renal/Kidney: Indicated as negative in the text.

#### **Overall Quality Determination**

**Study Citation:** Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-

Health Reproductive/Developmental

**Outcome(s):** 

Pregnancy rates of exposed females, pregnancy rates of females mated with exposed males, preimplantation loss, post-implantation loss, pup survival, pup Reported Health

Effect(s): weight and growth, structural teratology examinations, pup agitation in open space experiments

**Duration:** Reproductive/Developmental Mice- GD9-GD10 Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain	Metric		Rating	Comments	
Domain 1: Test Subst	tance				
	Metric 1:	Test Substance Identity	High	Test substance was identified 1,2-dichloroethane.	
	Metric 2:	Test Substance Source	Low	The source of the test substance was Beijing Chemical Plant Two. Batch/lot number was not provided.	
	Metric 3:	Test Substance Purity	High	The purity of test substance was reported as 98.5%.	
Domain 2: Test Desig	gn				
	Metric 4:	Negative and Vehicle Controls	Low	It is not clear if a negative control group was included.	
	Metric 5:	Positive Controls	N/A	A positive control was not needed.	
	Metric 6:	Randomized Allocation of Animals	Low	The study does not report how animals were allocated.	
Domain 3: Exposure	Characterization				
Domain S. Enposure	Metric 7:	Preparation and Storage of Test	Low	The preparation and storage of test substance were not reported.	
	Metric 8:	Substance Consistency of Exposure	Low	Details on exposure administration are insufficiently reported.	
	Metric 9:	Administration Reporting of Doses/Concentrations	Low	Actual concentrations were not reported.	
	Metric 10:	Exposure Frequency and Duration	Medium	Exposure frequency was 4 hours/day.	
	Metric 11:	Number of Exposure Groups and	Low	Only one concentration studied. No data are reported to evaluate responses.	
		Dose/Concentration Spacing			
	Metric 12:	Exposure Route and Method	Uninformative	There is no description of the inhalation chamber.	
Domain 4: Test Anim	nals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights and age were not reported.	
	Metric 14:	Adequacy and Consistency of Animal	Low	Husbandry conditions were not reported.	
		Husbandry Conditions			
	Metric 15:	Number of Animals per Group	Low	The number of animals/group was not reported.	
Domain 5: Outcome	Assessment				
	Metric 16:	Outcome Assessment Methodology	Low	Details on methodology were not reported.	
	Metric 17:	Consistency of Outcome Assessment	Low	There were no details regarding the execution of the study protocol.	
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported.	
	Metric 19:	Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.	
	Metric 20:	Negative Control Response	Low	The negative control responses were not reported.	

HERO ID: 200708 Table: 3 of 5

#### ... continued from previous page

Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-**Study Citation:** 

Reproductive/Developmental Health

**Outcome(s):** 

Reported Health Pregnancy rates of exposed females, pregnancy rates of females mated with exposed males, preimplantation loss, post-implantation loss, pup survival, pup

Effect(s): weight and growth, structural teratology examinations, pup agitation in open space experiments

**Duration:** Reproductive/Developmental Mice- GD9-GD10 Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200708

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable	Control		
Metric 21	: Confounding Variables in Test Design and Procedures	Low	Respiratory rates were not reported and are needed since the test substance is a respiratory irritant.
Metric 22	: Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.
Metric 23	: Data Presentation and Analysis	Low	No data or statistics were reported.
Metric 24	: Reporting of Data	Uninformative	No data are reported (negative or positive).

#### **Overall Quality Determination**

Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-

HERO ID: 200708 Table: 4 of 5

**Study Citation:** 

Reproductive/Developmental Health Outcome(s): Pregnancy rates of exposed females, pregnancy rates of females mated with exposed males, preimplantation loss, post-implantation loss, pup survival, pup Reported Health weight and growth, structural teratology examinations, pup agitation in open space experiments Effect(s): **Duration:** Reproductive/Developmental Mice-GD6-GD15 Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 200708 Domain Metric Comments Rating Domain 1: Test Substance Metric 1: Test Substance Identity High Test substance was identified 1.2-dichloroethane. Metric 2: Test Substance Source The source of the test substance was Beijing Chemical Plant Two. Batch/lot number was Low not provided. High Metric 3: Test Substance Purity The purity of test substance was reported as 98.5%. Domain 2: Test Design Metric 4: Negative and Vehicle Controls Low It is not clear if the animals were untreated or sham exposed. Metric 5: Positive Controls N/A A positive control was not needed. Metric 6: Randomized Allocation of Animals Low The study does not report how animals were allocated. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low The preparation and storage of test substance were not reported. Substance Consistency of Exposure Metric 8: Low Details on exposure administration are insufficiently reported. Administration Reporting of Doses/Concentrations Metric 9: Low Actual concentrations were not reported. **Exposure Frequency and Duration** Medium Metric 10: Exposure frequency was 4 hours/day. Metric 11: Number of Exposure Groups and Medium Minor limitations with the number of exposure groups (a full range or responses were Dose/Concentration Spacing not obtained). Exposure Route and Method Uninformative Metric 12: There is no description of the inhalation chamber. Domain 4: Test Animals Metric 13: **Test Animal Characteristics** Medium Starting body weights and age were not reported. Metric 14: Adequacy and Consistency of Animal Low Husbandry conditions were not reported. **Husbandry Conditions** Metric 15: Number of Animals per Group Low The number of animals/group was not reported. Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology Medium Details on methodology were not reported. Metric 17: Consistency of Outcome Assessment Low There were no details regarding the execution of the study protocol. Sampling Adequacy Metric 18: Low Details regarding sampling of outcomes were not reported. Metric 19: Blinding of Assessors N/A Blinding was not needed to assess outcomes. Metric 20: Negative Control Response Low The negative control responses were not reported. Continued on next page ...

HERO ID: 200708 Table: 4 of 5

1,1-Dichloroethane

#### ... continued from previous page

Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-**Study Citation:** 

Reproductive/Developmental Health

**Outcome(s):** 

Reported Health Pregnancy rates of exposed females, pregnancy rates of females mated with exposed males, preimplantation loss, post-implantation loss, pup survival, pup

Effect(s): weight and growth, structural teratology examinations, pup agitation in open space experiments

**Duration:** Reproductive/Developmental Mice-GD6-GD15 Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200708

Domain	Metric		Rating	Comments
Domain 6: Confounding / V	Variable Con	itrol		
M	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Respiratory rates were not reported and are needed since the test substance is a respiratory irritant.
M	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.
M	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed but not described adequately.
N	Metric 24:	Reporting of Data	Low	Some results are reported in text of results. Not adequately reported.

#### **Overall Quality Determination**

HERO ID: 200708 Table: 5 of 5

Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-**Study Citation:** Health Reproductive/Developmental Outcome(s): Reported Health Pregnancy rates of exposed females, pregnancy rates of females mated with exposed males, preimplantation loss, post-implantation loss, pup survival, pup weight and growth, structural teratology examinations, pup agitation in open space experiments Effect(s): **Duration:** Reproductive/Developmental Male rats- 7 days Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane **HERO ID:** 200708 Domain Metric Rating Comments Domain 1: Test Substance Metric 1: Test Substance Identity High Test substance was identified 1.2-dichloroethane. Metric 2: Test Substance Source Low The source of the test substance was Beijing Chemical Plant Two. Batch/lot number was not provided. Metric 3: Test Substance Purity High The purity of test substance was reported as 98.5%. Domain 2: Test Design Metric 4: Negative and Vehicle Controls Low It is not clear if the animals were untreated or sham exposed. Metric 5: Positive Controls Uninformative No positive controls are used for this dominant lethal study and no reference is made to historical positive controls from this laboratory. The OECD guideline for rodent dominant lethal studies (TG 478) states that "concurrent positive animal controls should always be used unless the laboratory has demonstrated proficiency in the conduct of the Metric 6: Randomized Allocation of Animals Low The study does not report how animals were allocated. Domain 3: Exposure Characterization Metric 7: Preparation and Storage of Test Low The preparation and storage of test substance were not reported. Substance Consistency of Exposure Metric 8: Low Details on exposure administration are insufficiently reported. Administration Reporting of Doses/Concentrations Metric 9: Low Actual concentrations were not reported. Study reports different concentration in the methods (0, 25 and 800 mg/m3) than what is reported in results (0, 20, 800 mg/m3). Metric 10: **Exposure Frequency and Duration** Medium Exposure frequency was 4 hours/day. Metric 11: Number of Exposure Groups and Medium Minor limitations with the number of exposure groups (a full range or responses were Dose/Concentration Spacing not obtained). Metric 12: Exposure Route and Method Uninformative There is no description of the inhalation chamber. Domain 4: Test Animals Metric 13: Test Animal Characteristics Medium Starting body weights and age were not reported. Metric 14: Adequacy and Consistency of Animal Low Husbandry conditions were not reported. **Husbandry Conditions** Number of Animals per Group Metric 15: Low The number of animals/group was not reported. Domain 5: Outcome Assessment Metric 16: Outcome Assessment Methodology Low Outcome methodology were not clearly reported. Metric 17: Consistency of Outcome Assessment Low There were no details regarding the execution of the study protocol. Continued on next page ...

Study Citation: Zhao, S.F., Bao, Y.S., Zhang, X.C. (1989). Studies on the effects of 1,2-dichloroethane on reproductive function. Zhonghua Yufang Yixue Zazhi 23(4):199-

202.

**Health** Reproductive/Developmental

**Outcome(s):** 

**Reported Health** Pregnancy rates of exposed females, pregnancy rates of females mated with exposed males, preimplantation loss, post-implantation loss, pup survival, pup

Effect(s): weight and growth, structural teratology examinations, pup agitation in open space experiments

**Duration:** Reproductive/Developmental Male rats- 7 days **Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 200708

Domain		Metric Rating		Comments	
N	Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported.	
N	Metric 19:	Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.	
N	Metric 20:	Negative Control Response	High	The negative control responses were reported and appropriate.	
Domain 6: Confounding / N	Variable Con Metric 21:		Low	Respiratory rates were not reported and are needed since the test substance is a respiratory irritant.	
N	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes dif- ferences unrelated to exposure.	
N	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed but not described adequately.	
N	Metric 24:	Reporting of Data	High	Data were reported for outcomes.	

# **Overall Quality Determination**

HERO ID: 94473 Table: 1 of 1

**Study Citation:** Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic

and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

**Reported Health** 

Tumor initiation assay: Skin, lung, stomach tumors

Effect(s):

**Duration:** Other (specify) Single Dose Tumor Initiator. Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Domain		Metric	Rating	Comments	
Domain 1: Test Substan	ce				
	Metric 1:	Test Substance Identity	High	Identified as 1,2-Dichloroethane; CASRN not provided; Structure (SMILES) reported.	
	Metric 2:	Test Substance Source	High	Test substance was obtained from a commercial source; the batch and lot number were not provided, Identity was independently verified by the laboratory performing the experiment (NMR)	
	Metric 3:	Test Substance Purity	Medium	The commercial-grade of the test substance was not reported. The laboratory conducted NMR analysis to confirm the identity and purity of the test substance. The text indicates that in some cases gas chromatograms were also done to substantiate the structure. The text generally states that these methods showed no marked impurities, but specific purities of each compound evaluated were not reported.	
Domain 2: Test Design					
Domain 2. Test Design	Metric 4:	Negative and Vehicle Controls	Low	Although they are discussed in the methods, it is unclear, based on data tables, whether a no treatment, and/or acetone vehicle-only control was included; however, a PMA-only control was included.	
	Metric 5:	Positive Controls	Medium	The study indicates a positive control was used, and reports mean survival time for this group, it does not specify what the positive control is.	
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.	
Damain 2. Evmasum Ch	ama atamizatian				
Domain 3: Exposure Ch		D C LC CT	т		
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation (in acetone) was described, however no details on storage, or when prepara- tions were made were not provided. Due to the volatility of the test substance, this could have a significant impact on results.	
	Metric 8:	Consistency of Exposure Administration	High	For tumor initiation experiments, the test substance was only administered once. Control animals concurrently received vehicle alone, the positive control, or were left untreated.	
	Metric 9:	Reporting of Doses/Concentrations	Low	The dose was reported in mg/application/mouse or 126 mg in 0.2mL of acetone per mouse. No information on animal body weights was provided.	
	Metric 10:	Exposure Frequency and Duration	High	For this type of study (tumor initiation study), the single applied dose is appropriate.	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The appropriateness of the dose is uncertain; no increase in the number of tumors was observed; positive and negative controls were reported to be valid.	

Study Citation:	Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic
	and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

Health

Cancer/Carcinogenesis

**Outcome(s):** 

Reported Health

Tumor initiation assay: Skin, lung, stomach tumors

**Effect(s):** 

Duration:Other (specify) Single Dose Tumor Initiator.Chemical:1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

HERO ID:	94473			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Uninformative	The Dermal route of exposure is acceptable for the study type, however, the method of exposure did not take into account the volatility of the test substance. Based on the information provided. The test substance (in acetone) was pipetted onto clipped skin. The methods provide no indications suggesting the use of a Finn chamber or occlusive conditions to prevent evaporation. This is considered to be unacceptable for a volatile compound, especially since treatment was performed in a ventilated hood.
Domain 4: Test Animal	ls			
	Metric 13:	Test Animal Characteristics	Low	Animal species, strain, source, sex, and age were reported. Starting body weights were not included. Only a single-sex (females) was used for the experimental group without justification.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some, but not all animal husbandry conditions were reported. Light-dark cycles were not included.
	Metric 15:	Number of Animals per Group	Medium	The study reports the use of 30 animals females in the treatment group, 100 animals in the no-treatment group and 90-120 mice in two PMA only groups (sexes not specified).
Domain 5: Outcome As	ssessment			
	Metric 16:	Outcome Assessment Methodology	Medium	Criteria for outcome assessment (formation of papillomas) was minimally described. Additional details were available in a cited reference.
	Metric 17:	Consistency of Outcome Assessment	Low	The duration of animal observations for tumors is not entirely clear. A footnote in a dat table indicates that (for a list of chemicals), the "duration of the test and median survivatimes ranged from 428 to 576 days. The median survival time for the positive control was 376 days, but similar information was not provided for the PMA alone group, or thuntreated controls. Therefore, it is unclear if there was any consistency in observation time (and thus outcome assessment) between the experimental and untreated control group.
	Metric 18:	Sampling Adequacy	High	All animals were monitored for development of papillomas.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology review.
	Metric 20:	Negative Control Response	Low	For the tumor initiation experiment. The number of tumors in no-treatment controls (even if zero) is not reported. However, tumor incidence from PMA only controls was included.
Domain 6: Confoundin	g / Variable Co	ntrol		
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report information to determine confounding
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.

HERO ID: 94473 Table: 1 of 1

#### ... continued from previous page

Study Citation: Duuren, B.L., Goldschmidt, B.M., Loewengart, G., Smith, A.C., Melchionne, S., Seidman, I., Roth, D. (1979). Carcinogenicity of halogenated olefinic

and aliphatic hydrocarbons in mice. Journal of the National Cancer Institute 63(6):1433-1439.

**Health** Cancer/Carcinogenesis

**Outcome(s):** 

Reported Health

Tumor initiation assay: Skin, lung, stomach tumors

**Effect(s):** 

**Duration:**Other (specify) Single Dose Tumor Initiator.**Chemical:**1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 94473

Domain	Metric		Rating	Comments	
Metr	ic 23: Data	Presentation and Analysis	High	Significance values for tumor occurrence were calculated using chi-square analysis; Incidence data were also provided to conduct independent statistical analysis.	
Metr	ic 24: Repo	ting of Data	High	Although there were deficiencies in test methods, and details provided, of the data collected, data reporting was adequate. A limited number of outcomes were included in this study (primarily tumors only). Although it was initially presumed based on the methods that a no-treatment control was used, this data is not reported for the tumor initiation study. It is unclear whether this is a data reporting issue, or whether this control group was actually not included. The negative control metric was already downgraded due to this uncertainty, so it is not reflected here.	

# **Overall Quality Determination**

Study Citation: Health	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride. Irritation (eye irritation)						
Outcome(s): Reported Health Effect(s):	Eye irritation (signs of redness and chemosis); skin irritation (signs of erythema, edema, or corrosiveness)						
Duration: Chemical: HERO ID:	Other (specify) Acute - Eye irritation 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 6569955						
Domain	0309933	Metric	Rating	Comments			
Domain 1: Test Substan	ce	Wette	Rating	Comments			
	Metric 1: Metric 2:	Test Substance Identity Test Substance Source	High High	Test material: 1,2-dichloroethane (ethylene dichloride). The CASRN was provided.  The test material was obtained from "the specialty chemical division" of the Stauffer			
	Metric 3:	Test Substance Purity	Low	Chemical Company. The purity was not reported.			
Domain 2: Test Design							
	Metric 4:	Negative and Vehicle Controls	High	Untreated eyes served as the negative controls.			
	Metric 5:	Positive Controls	N/A	Not necessary for the study type.			
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.			
D : 4 E							
Domain 3: Exposure Ch		D (* 16) CT (	M. P.				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Limited details were provided but 0.1 mL of the test material was administered to the eye without dilution. Details on storage were not reported, although this is unlikely to have a major impact on an acute duration study.			
	Metric 8:	Consistency of Exposure	High	Available information suggests all animals received the same treatment.			
	Metric 9:	Administration Reporting of Doses/Concentrations	High	The dose (10 mg) was clearly reported.			
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type			
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	Only one exposure concentration was used in this study. This was appropriate for the study type.			
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and were suited to the test substance.			
Domain 4: Test Animals							
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, and initial body weights were provided. The age, sex, and source of the animals was not specified.			
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.			
	Metric 15:	Number of Animals per Group	Medium	The study used 5 animals/group.			
Domain 5: Outcome Ass	Domain 5: Outcome Assessment						
Continued on next page							

**Study Citation:** 

Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.

Health

Irritation (eye irritation)

**Outcome(s):** 

Reported Health

Eye irritation (signs of redness and chemosis); skin irritation (signs of erythema, edema, or corrosiveness)

Effect(s):

**Duration:** Other (specify) Acute - Eye irritation

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6569955

Domain	Metric	Rating	Comments
Metric 16:	Outcome Assessment Methodology	Medium	Some details of the outcome assessment were not provided (e.g., method of scoring irritation). Additionally, animals are typically observed for 7 days in an eye irritation study. However, the lack of observation past 72 hours may not have been necessary because all effects were reversible. Current guidelines state that the eyes should be examined after 1 h.
Metric 17:	Consistency of Outcome Assessment	High	The outcomes were assessed consistently for each animal (e.g., same time points).
Metric 18:	Sampling Adequacy	High	All animals were examined.
Metric 19:	Blinding of Assessors	N/A	Not necessary for the study type.
Metric 20:	Negative Control Response	Low	The biological response of the negative control groups were not reported. It is assumed no irritation was observed.
Domain 6: Confounding / Variable Co	ontrol		
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report information to determine confounding, but this is unlikely to have an effect on the outcomes of interest.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	N/A	Statistical methods are not necessary for this outcome of interest.
Metric 24:	Reporting of Data	Low	Neither mean nor individual irritation scores were provided. Limited results were described in the text.

## **Overall Quality Determination**

#### Medium

**Study Citation:** Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.

Health

Irritation (Skin irritation)

**Outcome(s):** 

**Reported Health** 

**Effect(s):** 

Eye irritation (signs of redness and chemosis); skin irritation (signs of erythema, edema, or corrosiveness)

**Duration:** 

Other (specify) Acute - Skin irritation

**Chemical:** 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

0307733			
	Metric	Rating	Comments
nce			
Metric 1:	Test Substance Identity	High	Test material: 1,2-dichloroethane (ethylene dichloride). The CASRN was provided.
Metric 2:	Test Substance Source	High	The test material was obtained from "the specialty chemical division" of the Stauffer Chemical Company.
Metric 3:	Test Substance Purity	Low	The purity was not reported.
1			
Metric 4:	Negative and Vehicle Controls	N/A	Not necessary for the study type.
Metric 5:	Positive Controls	N/A	Not necessary for the study type.
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
'haracterization			
Metric 7:	Preparation and Storage of Test	Low	No information on preparation was provided.
Metric 8:	Substance Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported in the report itself. However, the cited guideline states a detailed procedure.
Metric 9:	Reporting of Doses/Concentrations	Low	The dose was not reported. However, the guideline that they cite at the time does not require a dose, but an amount of the material to be added to the skin. "Liquid test materials (0.5 milliliter) and/or solid or semisolid test materials (0.5 gram) are introduced under a 1.5 by 1.5 inch 12-ply gauze patch which is secured in place by two H x 4 inch strips of adhesive tape in the form of an X.
Metric 10:	Exposure Frequency and Duration	High	The guideline states exposure should be first checked at 4 h, 24 h, and 48 h.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	Only one exposure concentration was used in this study. This was appropriate for the study type.
Metric 12:	Exposure Route and Method	Medium	The route was appropriate, but no additional details on the method (e.g., occluded or non-occluded, or location, coverage area etc.,) were provided. However, the guideline details the placement and preparation for administration, and it is assumed that this was followed.
ls			
Metric 13:	Test Animal Characteristics	Low	Species and strain were the only test animal parameters reported
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
Metric 15:	Number of Animals per Group	Medium	The number of animals used was appropriate.
ssessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment (Draize method) was appropriate for the study type.
	Metric 1: Metric 2: Metric 3:  Metric 4: Metric 5: Metric 6:  Characterization Metric 7: Metric 8: Metric 9:  Metric 10: Metric 11: Metric 12:  Is Metric 13: Metric 14: Metric 15:  Ssessment	Metric 1: Test Substance Identity Metric 2: Test Substance Source  Metric 3: Test Substance Purity  Metric 4: Negative and Vehicle Controls Metric 5: Positive Controls Metric 6: Randomized Allocation of Animals  Characterization Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Administration Metric 9: Reporting of Doses/Concentrations  Metric 10: Exposure Frequency and Duration Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method  Is Metric 13: Test Animal Characteristics Metric 14: Adequacy and Consistency of Animal Husbandry Conditions Metric 15: Number of Animals per Group	Metric 1: Test Substance Identity High Metric 2: Test Substance Source High Metric 3: Test Substance Purity Low  Metric 3: Test Substance Purity Low  Metric 4: Negative and Vehicle Controls N/A Metric 5: Positive Controls N/A Metric 6: Randomized Allocation of Animals Low  Characterization Metric 7: Preparation and Storage of Test Substance Metric 8: Consistency of Exposure Low Administration Metric 9: Reporting of Doses/Concentrations Low  Metric 10: Exposure Frequency and Duration High Metric 11: Number of Exposure Groups and Dose/Concentration Spacing Metric 12: Exposure Route and Method Medium  Metric 13: Test Animal Characteristics Low Metric 14: Adequacy and Consistency of Animal Low Husbandry Conditions Metric 15: Number of Animals per Group Medium

HERO ID: 6569955 Table: 2 of 2

#### ... continued from previous page

**Study Citation:** Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride. Irritation (Skin irritation)

Health

**Outcome(s):** 

Reported Health

Eye irritation (signs of redness and chemosis); skin irritation (signs of erythema, edema, or corrosiveness)

Effect(s): **Duration:** 

Other (specify) Acute - Skin irritation

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

**HERO ID:** 6569955

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	High	The outcomes were assessed consistently for each animal (e.g., same time points).
	Metric 18:	Sampling Adequacy	High	All animals were examined.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for the study type.
	Metric 20:	Negative Control Response	N/A	Negative controls were not used in this study.
Domain 6: Confound	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report information to determine confounding, but this is unlikely to have an effect on the outcomes of interest.
	Metric 21:	e	Medium Medium	The study did not report information to determine confounding, but this is unlikely to have an effect on the outcomes of interest.  There was no information either to support or dismiss the suggestion that there were
	Wietire 22.	Exposure Exposure	Wedium	differences among groups in animal attrition or health outcomes unrelated to exposur (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical methods are not necessary for this outcome of interest.
	Metric 24:	Reporting of Data	High	Individual animal scores at each timepoint were reported.

# **Overall Quality Determination**

### Medium