United States
Environmental Protection Agency

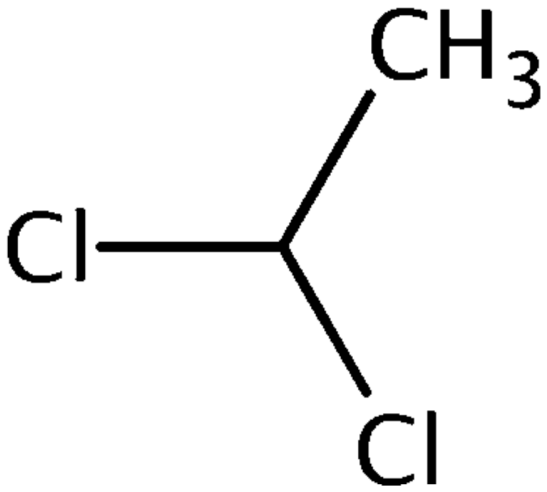
July 2024
Office of Chemical Safety and
Pollution Prevention

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



July 2024

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-DCA, 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 trans-1,2-dichloroethylene. The acronym 1,2-DCP refers to the chemical 1,2-dichloropropane.

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Isomer: Dichloroethane

Isomer: dichloroethane

Isomer: 1,2-Dichloroethane

Acute (less than or equal to 24 hr)

Study Citation:	Dow Chemical, (1947). Results of range-finding toxicological studies on Ethylidene Dichloride.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
Duration:	Acute (less than or equal to 24 hr) Acute-oral
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973137

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Design				
	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				
	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 gavage volume)
	Metric 9:	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 Animals				
	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.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Low	Animals were assessed for mortality, but it was not specified how long animals were observed post-exposure.

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Study Citation:	Dow Chemical, (1947). Results of range-finding toxicological studies on Ethylidene Dichloride.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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: Confounding / Variable Control				
	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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)
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 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	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 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	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.
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 Assessment				
	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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)
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 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: Confounding / Variable Control				
	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.

Overall Quality Determination 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 Outcome(s):	Nutritional/Metabolic
Reported Health 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- Parent compound
HERO ID:	200479

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 body 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	A single gavage dose is appropriate for 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 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 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.
	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 Outcome(s):	Nutritional/Metabolic
Reported Health 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- 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: Confounding / Variable Control				
	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 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 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

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Decreased absolute liver weight (1,1,2-TCE only)
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 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 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	A single gavage dose is appropriate for 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 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 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.

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Decreased absolute liver weight (1,1,2-TCE only)
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: Confounding / Variable Control			
	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

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):	Neurological/Behavioral
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:	Acute (less than or equal to 24 hr) Single dose
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 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 Characterization				
	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.
	Metric 12:	Exposure Route and Method	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 acute study, the rats were male and weighed 250-300 g. Rats were obtained from Harlan (Indianapolis, IN).

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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):	Neurological/Behavioral
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:	Acute (less than or equal to 24 hr) Single dose
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 Assessment				
	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 / Variable 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. 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

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):	Mortality
Reported Health Effect(s):	The number of deaths per treatment group.
Duration:	Acute (less than or equal to 24 hr) Single dose
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 Characterization				
	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				
	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.

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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):	Mortality
Reported Health Effect(s):	The number of deaths per treatment group.
Duration:	Acute (less than or equal to 24 hr) Single dose
Chemical:	1,1-Dichloroethane- Parent compound
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 Control				
	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 22:	Health Outcomes Unrelated to Exposure	High	In the acute study, the number of fatalities was 0/8 at 0 mg/kg bw, 1000 mg/kg bw, 2000 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

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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary glucose and protein; renal histopathology
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
Domain 1: Test Substance				
	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 Characterization				
	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 Dose/Concentration Spacing	Medium	There were minor limitation in dose 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 Husbandry Conditions	Low	Husbandry conditions were not reported.
	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 Assessment				
	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.

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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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary glucose and protein; renal histopathology
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: 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 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 Pharmacology 7(1):37-44.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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
Domain 1: Test Substance				
	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 Characterization				
	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 Dose/Concentration Spacing	Medium	There were minor limitation in dose 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 Husbandry Conditions	Low	Husbandry conditions were not reported.
	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 Assessment				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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 / 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 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

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):	Mortality
Reported Health Effect(s):	The number of deaths per treatment group.
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				
	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 necessary in the subacute study.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characterization				
	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 are not necessary since this was 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	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				
	Metric 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).
	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 Outcome(s):	Mortality
Reported Health Effect(s):	The number of deaths per treatment group.
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: Confounding / Variable 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 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

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):	Immune/Hematological; Reproductive/Developmental;
Reported Health Effect(s):	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				
	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				
	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 5.1 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 Characterization				
	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 doses were reported, but analytical concentrations were not necessary based on oral gavage.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Doses were administered the test substance once daily for up to 10 days.
	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 subacute study, the rats were 250-300 g. The animals were obtained from Harlan (Indianapolis, IN).

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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):	Immune/Hematological; Reproductive/Developmental;
Reported Health Effect(s):	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
	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 Assessment				
	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: Confounding / Variable Control				
	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 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 Outcome(s):	Renal/Kidney
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:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 needed based on the study type.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characterization				
	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 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:	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):	Renal/Kidney
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:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 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 reported 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.
Domain 6: Confounding / Variable 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	High	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

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):	Hepatic/Liver
Reported Health Effect(s):	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:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 Characterization				
	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:	Exposure Route and Method	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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	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:	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	Clinical chemistry, liver 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	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.
	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	The control group did not exhibit any abnormal liver effects.
Domain 6: Confounding / Variable Control				
	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

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):	Nutritional/Metabolic
Reported Health Effect(s):	Reduced body weight gain in subacute and subchronic studies
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				
	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 Characterization				
	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				
	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.

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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):	Nutritional/Metabolic
Reported Health Effect(s):	Reduced body weight gain in subacute and subchronic studies
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	High	Body weight measurements were taken.
	Metric 17:	Consistency of Outcome Assessment	High	Body weights were measured for all treatment groups
	Metric 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.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary.
	Metric 20:	Negative Control Response	High	The control group did not exhibit any abnormal body weight effects.
Domain 6: Confounding / Variable 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 23:	Data Presentation and Analysis	High	The study authors used one-way ANOVA to evaluate the statistical significance of DCE-induced changes.
	Metric 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

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):	Adrenal (Adrenal)
Reported Health Effect(s):	Adrenals histopathology were evaluated and no effects were found.
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				
	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 Characterization				
	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				
	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):	Adrenal (Adrenal)
Reported Health Effect(s):	Adrenals histopathology were evaluated and no effects were found.
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	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.
Domain 6: Confounding / Variable Control				
	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.

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 Outcome(s):	Neurological/Behavioral
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 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 Characterization				
	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				
	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.

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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):	Neurological/Behavioral
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 / Variable 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 23:	Data Presentation and Analysis	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 Outcome(s):	Lung/Respiratory
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:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 Characterization				
	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				
	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.
	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):	Lung/Respiratory
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:	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	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: Confounding / Variable Control				
	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.
	Metric 24:	Reporting of Data	High	Negative findings were reported qualitatively.

Overall Quality Determination High

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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary glucose and protein; renal histopathology
Duration:	Short-term (>1-30 days) Short-term- 3 days
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	64411

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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 Dose/Concentration Spacing	Medium	The one dose studied was the highest one that did not cause lethality.
	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 mice 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	The number of animals/group were not reported.
Domain 5: Outcome Assessment				
	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.

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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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary glucose and protein; renal histopathology
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 / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Potential confounding variables 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	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 rats. Toxicology and Applied Pharmacology 28(3):452-464.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver weights, gross appearance/pathology and SGPT/ALT activity
Duration:	Short-term (>1-30 days) 10 days
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 Characterization				
	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.

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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):	Hepatic/Liver
Reported Health Effect(s):	Liver weights, gross appearance/pathology and SGPT/ALT activity
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 Animals				
	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 Assessment				
	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: Confounding / Variable Control				
	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.

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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):	Hepatic/Liver
Reported Health Effect(s):	Liver weights, gross appearance/pathology and SGPT/ALT activity
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.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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				
	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				
	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. 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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
Duration:	Subchronic (>30-91 days) Up to 6 weeks - rabbits
Chemical:	1,1-Dichloroethane- 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 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: Confounding / Variable Control				
	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

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)
Duration:	Subchronic (>30-91 days) 7 Weeks (promotion protocol)
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	200479

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	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 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	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				
	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 was appropriate and sensitive for tumor promotion potential.
	Metric 17:	Consistency of Outcome Assessment	High	Timing of necropsy was consistent across groups.
	Metric 18:	Sampling Adequacy	High	Sample size (n = 7-10) was adequate for assessment of tumor promotion 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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)
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	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: Confounding / Variable Control				
	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

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Decreased body weight gain (1,1,2-TCE only)
Duration:	Subchronic (>30-91 days) 7 Weeks (promotion protocol)
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	200479

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 body 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 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				
	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Decreased body weight gain (1,1,2-TCE only)
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: Confounding / Variable Control				
	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

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Decreased absolute liver weight (1,1,2-TCE only)
Duration:	Subchronic (>30-91 days) 7 Weeks (promotion protocol)
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	200479

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 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 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				
	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.

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Decreased absolute liver weight (1,1,2-TCE only)
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: Confounding / Variable Control				
	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 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

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):	Immune/Hematological; Adrenal; Reproductive/Developmental; Gastrointestinal;
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;
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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				

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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):	Immune/Hematological; Adrenal; Reproductive/Developmental; Gastrointestinal;
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;
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- 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.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Organ weight measurement and histopathology were performed.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome assessment was consistent for all treatment groups
	Metric 18:	Sampling Adequacy	Low	Immune/Hematological: For histopathology, samples were collected from all animals, 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.
	Metric 19:	Blinding of Assessors	High	Immune/Hematological: For histopathology, the study states that tissue specimens were 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: Confounding / Variable Control				
	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.

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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):	Immune/Hematological; Adrenal; Reproductive/Developmental; Gastrointestinal;
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;
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

Domain	Metric	Rating	Comments
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 Outcome(s):	Lung/Respiratory
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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 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 Characterization				
	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				
	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.

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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):	Lung/Respiratory
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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

Domain	Metric		Rating	Comments
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Organ weight measurement and histology were performed.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was consistent for all treatment groups
	Metric 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.
	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	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.
Domain 6: Confounding / Variable 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 23:	Data Presentation and Analysis	High	While the authors do not appear to have performed statistical analysis on pulmonary inflammation, incidence data are provided.
	Metric 24:	Reporting of Data	High	Findings were reported qualitatively and quantitatively in Table 3.

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 Outcome(s):	Mortality; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: The number of deaths per treatment group.; Nutritional/Metabolic: Reduced body weight gain in subacute and subchronic studies;
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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 Characterization				
	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:	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):	Mortality; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: The number of deaths per treatment group.; Nutritional/Metabolic: Reduced body weight gain in subacute and subchronic studies;
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- 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 15 rats were used in the subchronic study.
Domain 5: Outcome Assessment				
	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: Confounding / Variable Control				
	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 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 Outcome(s):	Renal/Kidney
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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 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 Characterization				
	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 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 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 Outcome(s):	Renal/Kidney
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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	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 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: Confounding / Variable 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	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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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):	Renal/Kidney
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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

Domain	Metric	Rating	Comments
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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 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 Characterization				
	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 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 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.

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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):	Hepatic/Liver
Reported Health Effect(s):	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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

Domain	Metric		Rating	Comments
Domain 5: Outcome Assessment				
	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 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 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 Outcome(s):	Neurological/Behavioral
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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

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 1.3 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 Characterization				
	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 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 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.

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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):	Neurological/Behavioral
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:	Subchronic (>30-91 days) 13 weeks
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	644914

Domain	Metric		Rating	Comments
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Low	Outcome assessment methodology for CNS depression was not described.
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding outcome assessment protocol were not reported.
	Metric 18:	Sampling Adequacy	Low	Details of sampling for this endpoint were 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	No effects were reported in the control group
Domain 6: Confounding / Variable 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	The study did not provide sufficient information to determine potential for confounding, but no differences among groups were reported.
	Metric 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.
	Metric 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):1-107.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight (6 week and 78 week study), food consumption (78 week study only)
Duration:	Subchronic (>30-91 days) 6 weeks- Mouse
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).
	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 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 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:	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight (6 week and 78 week study), food consumption (78 week study only)
Duration:	Subchronic (>30-91 days) 6 weeks- Mouse
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	646679

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 (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: Confounding / Variable Control				
	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	N/A	A statistical analysis of body weight data does not appear to have been performed, however, study authors report "no mean body weight depression was observed in mice" so statistical analysis was not necessary.
	Metric 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.
Health Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: survival; Mortality: survival;
Duration:	Subchronic (>30-91 days) 6 weeks- Mouse
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.
	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 Characterization				
	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.

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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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: survival; Mortality: survival;
Duration:	Subchronic (>30-91 days) 6 weeks- Mouse
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	646679

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: Outcome 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: Confounding / Variable Control				
	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 independent 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).

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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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: survival; Mortality: survival;
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**	

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight (6 week and 78 week study), food consumption (78 week study only)
Duration:	Subchronic (>30-91 days) 6 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).
	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 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 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:	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				

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight (6 week and 78 week study), food consumption (78 week study only)
Duration:	Subchronic (>30-91 days) 6 weeks-rat
Chemical:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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 enabling an independent statistical analysis were not provided.
	Metric 24:	Reporting of Data	Uninformative	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.

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 Outcome(s):	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:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
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 1,1-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 3: Exposure Characterization				
	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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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):	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:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
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				
	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:	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):	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:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1937626

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 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:	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):	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:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1937626

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 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 experimental period.
	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:	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):	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:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1937626

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 reported (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: Confounding / Variable Control				
	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:	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):	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:	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	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).; 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, 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 weights, or kidney 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 status, kidney weights, or kidney histology (clearly negative findings across groups).

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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 Outcome(s):	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:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1937626

Domain	Metric	Rating	Comments
	Metric 24: Reporting of Data	Medium	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)

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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 Outcome(s):	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:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology
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:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
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 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				

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology
Duration:	Chronic (>91 days) 26 weeks - cats
Chemical:	1,1-Dichloroethane- Parent compound
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 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 groups). The legend to Figure 3 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.
	Metric 18:	Sampling Adequacy	High	Liver 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	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 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 were no apparent effects on liver enzymes, bromosulphthalein retention, liver weights, or liver histology (clearly negative findings across groups).

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Activities of ALT and AST (rats, rabbits, and cats), bromsulphthalein test (rabbits and cats), liver weight, and liver histology
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

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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
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:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
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 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				

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
Duration:	Chronic (>91 days) 26 weeks - cats
Chemical:	1,1-Dichloroethane- Parent compound
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 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 weight loss was due to intercurrent infection.
Domain 6: Confounding / Variable Control				
	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 (biological significance can be assessed as a >10% change in body weights from controls).

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
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	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 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). 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 general condition after 23 weeks and cats (in both groups) with infection.

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 Outcome(s):	Renal/Kidney
Reported Health 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").
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:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
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 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				

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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 Outcome(s):	Renal/Kidney
Reported Health 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").
Duration:	Chronic (>91 days) 26 weeks - cats
Chemical:	1,1-Dichloroethane- Parent compound
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 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 Control				
	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 analyses.

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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 Outcome(s):	Renal/Kidney
Reported Health 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").
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	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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: Mortality; Mortality: Mortality;
Duration:	Chronic (>91 days) 26 weeks - rabbits
Chemical:	1,1-Dichloroethane- Parent compound
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 1,1-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 3: Exposure Characterization				
	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				

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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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: Mortality; Mortality: Mortality;
Duration:	Chronic (>91 days) 26 weeks - rabbits
Chemical:	1,1-Dichloroethane- Parent compound
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).
	Metric 15:	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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: Mortality; Mortality: Mortality;
Duration:	Chronic (>91 days) 26 weeks - rabbits
Chemical:	1,1-Dichloroethane- Parent compound
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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
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 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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
Duration:	Chronic (>91 days) 26 weeks - cats
Chemical:	1,1-Dichloroethane- Parent compound
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 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: Confounding / Variable Control				
	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

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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
Duration:	Chronic (>91 days) 26 weeks - guinea pigs
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:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
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 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				

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
Duration:	Chronic (>91 days) 26 weeks - guinea pigs
Chemical:	1,1-Dichloroethane- 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 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: Confounding / Variable Control				
	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, "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

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):	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").;
Duration:	Chronic (>91 days) 26 weeks - guinea pigs
Chemical:	1,1-Dichloroethane- Parent compound
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 1,1-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 3: Exposure Characterization				
	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				

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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 Outcome(s):	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").;
Duration:	Chronic (>91 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 Assessment				
	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: Confounding / Variable Control				
	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).

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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 Outcome(s):	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").;
Duration:	Chronic (>91 days) 26 weeks - guinea pigs
Chemical:	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

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):	Immune/Hematological; Immune/Hematological;
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);
Duration:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
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 1,1-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 3: Exposure Characterization				
	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				

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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 Outcome(s):	Immune/Hematological; Immune/Hematological;
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);
Duration:	Chronic (>91 days) 26 weeks - rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO 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 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 Assessment				
	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.
	Metric 18:	Sampling Adequacy	High	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	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 to be applicable to all the laboratory species tested in the study.
Domain 6: Confounding / Variable Control				
	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:	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):	Immune/Hematological; Immune/Hematological;
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);
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

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):	Immune/Hematological
Reported Health Effect(s):	Blood counts - specific parameters not specified (rats, rabbits, and cats only)
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:	Test Substance Purity	High	The purity of 1,1-dichloroethane was about 99%.
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 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				

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Blood counts - specific parameters not specified (rats, rabbits, and cats only)
Duration:	Chronic (>91 days) 26 weeks - cats
Chemical:	1,1-Dichloroethane- Parent compound
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 Assessment				
	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 Control				
	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.

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Blood counts - specific parameters not specified (rats, rabbits, and cats only)
Duration:	Chronic (>91 days) 26 weeks - cats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1937626

Domain	Metric	Rating	Comments
Overall Quality Determination		**Uninformative**	

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 Outcome(s):	Cancer/Carcinogenesis
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
Domain 1: Test Substance				
	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	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 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 Administration	High	Water was available ad libitum across groups
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
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 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 Animals				
	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 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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
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

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence
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 Substance				
	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 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 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 Administration	High	Water was available ad libitum across groups
	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	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence
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 Animals				
	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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence
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

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; water intake
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 Substance				
	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 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 Administration	High	Water was available ad libitum across groups
	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				

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; water intake
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 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 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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; water intake
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 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

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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 Substance				
	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 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 Administration	High	Water was available ad libitum across groups
	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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 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	No mortalities were observed in negative control groups
Domain 6: Confounding / Variable Control				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; body length
Duration:	Chronic (>91 days) 6 months; dogs
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

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				
	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 guideline 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				
	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)

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; body length
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: Confounding / Variable Control				
	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

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Survival
Duration:	Chronic (>91 days) 6 months; dogs
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

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				
	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 guideline 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				
	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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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Survival
Duration:	Chronic (>91 days) 6 months; dogs
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

Domain	Metric		Rating	Comments
Domain 5: Outcome 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: Confounding / Variable Control				
	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 Quality Determination Low

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Hepatic/Liver; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health Effect(s):	Hepatic/Liver: Live weights, histopathology; Reproductive/Developmental (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;
Duration:	Chronic (>91 days) 6 months; dogs
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

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 Characterization				
	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				
	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.

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Hepatic/Liver; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health Effect(s):	Hepatic/Liver: Live weights, histopathology; Reproductive/Developmental (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;
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:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Hepatic/Liver; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health Effect(s):	Hepatic/Liver: Live weights, histopathology; Reproductive/Developmental (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;
Duration:	Chronic (>91 days) 6 months; dogs
Chemical:	1,1-Dichloroethane- Parent compound
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.; 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.
	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: Confounding / Variable 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	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.

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Hepatic/Liver; Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health Effect(s):	Hepatic/Liver: Live weights, histopathology; Reproductive/Developmental (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;
Duration:	Chronic (>91 days) 6 months; dogs
Chemical:	1,1-Dichloroethane- Parent compound
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.; 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**

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; body length
Duration:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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				
	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 Animals				
	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

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; body length
Duration:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

Domain	Metric		Rating	Comments
Domain 5: Outcome 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: Confounding / Variable Control				
	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 mid-study), 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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
Duration:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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				
	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 Animals				
	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

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Survival
Duration:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

Domain	Metric		Rating	Comments
Domain 5: Outcome 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: Confounding / Variable Control				
	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

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Kidney weights and histopathology; serum BUN
Duration:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

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				
	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 Animals				
	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,

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Kidney weights and histopathology; serum BUN
Duration:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

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 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 end-points).
	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: Confounding / Variable Control				
	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 mid-study), 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 Outcome(s):	Reproductive/Developmental; Hepatic/Liver; Endocrine; Immune/Hematological; Lung/Respiratory; Cardiovascular;
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:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

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 Characterization				
	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?

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Reproductive/Developmental; Hepatic/Liver; Endocrine; Immune/Hematological; Lung/Respiratory; Cardiovascular;
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:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
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.; 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 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 Animals				
	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 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
	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%).

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Reproductive/Developmental; Hepatic/Liver; Endocrine; Immune/Hematological; Lung/Respiratory; Cardiovascular;
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:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973131

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable 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 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

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Renal/Kidney; Lung/Respiratory; endocrine (endocrine); Skin/Connective Tissue; Cancer/Carcinogenesis; Gastrointestinal; Reproductive/Developmental; 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:	Chronic (>91 days) 78 weeks- mouse
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.
	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 Characterization				
	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	All Outcomes: Mice were treated with test substance 5 days/week for 78 weeks.
	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.

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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 Outcome(s):	Renal/Kidney; Lung/Respiratory; endocrine (endocrine); Skin/Connective Tissue; Cancer/Carcinogenesis; Gastrointestinal; Reproductive/Developmental; 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:	Chronic (>91 days) 78 weeks- mouse
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	646679

Domain		Metric	Rating	Comments
Domain 4: Test Animals				
	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	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: Confounding / Variable Control				
	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

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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 Outcome(s):	Renal/Kidney; Lung/Respiratory; endocrine (endocrine); Skin/Connective Tissue; Cancer/Carcinogenesis; Gastrointestinal; Reproductive/Developmental; 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:	Chronic (>91 days) 78 weeks- mouse
Chemical:	1,1-Dichloroethane- 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 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.
Health Outcome(s):	Mortality
Reported Health Effect(s):	survival
Duration:	Chronic (>91 days) 78 weeks- mouse
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).
	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 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 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 carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Mortality
Reported Health Effect(s):	survival
Duration:	Chronic (>91 days) 78 weeks- mouse
Chemical:	1,1-Dichloroethane- 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	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: Confounding / Variable Control				
	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	Survival data were presented graphically for all control and treatment groups by sex.

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.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver histopathology and gross pathology
Duration:	Chronic (>91 days) 78 weeks- mouse
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).
	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 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 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 carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver histopathology and gross pathology
Duration:	Chronic (>91 days) 78 weeks- mouse
Chemical:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Thyroid
Reported Health Effect(s):	Thyroid histopathology and gross pathology
Duration:	Chronic (>91 days) 78 weeks- mouse
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).
	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 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 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 carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Thyroid
Reported Health Effect(s):	Thyroid histopathology and gross pathology
Duration:	Chronic (>91 days) 78 weeks- mouse
Chemical:	1,1-Dichloroethane- 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.
	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: Confounding / Variable Control				
	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

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight (6 week and 78 week study), food consumption (78 week study only)
Duration:	Chronic (>91 days) 78 weeks- mouse
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).
	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 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 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 carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight (6 week and 78 week study), food consumption (78 week study only)
Duration:	Chronic (>91 days) 78 weeks- mouse
Chemical:	1,1-Dichloroethane- 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	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 Control				
	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.

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.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Bone marrow, spleen, lymph nodes, thymus histopathology and gross pathology
Duration:	Chronic (>91 days) 78 weeks- mouse
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).
	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 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 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 carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Bone marrow, spleen, lymph nodes, thymus histopathology and gross pathology
Duration:	Chronic (>91 days) 78 weeks- mouse
Chemical:	1,1-Dichloroethane- 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	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: Confounding / Variable Control				
	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

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	endocrine (endocrine)
Reported Health Effect(s):	Pituitary, pancreas and adrenal gland 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 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	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				
	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				

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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 Outcome(s):	endocrine (endocrine)
Reported Health Effect(s):	Pituitary, pancreas and adrenal gland histopathology and gross pathology
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	Low	Not necessary for initial histology review.
	Metric 20:	Negative Control Response	High	Negative control response was adequate.
Domain 6: Confounding / Variable Control				
	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 — Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Cardiovascular; Neurological/Behavioral; Hepatic/Liver;
Reported Health Effect(s):	Cardiovascular: Heart histopathology and gross pathology; Neurological/Behavioral: Brain histopathology and gross pathology; clinical observations; 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 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.
	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 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 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.

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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 Outcome(s):	Cardiovascular; Neurological/Behavioral; Hepatic/Liver;
Reported Health Effect(s):	Cardiovascular: Heart histopathology and gross pathology; Neurological/Behavioral: Brain histopathology and gross pathology; clinical observations; 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 Animals				
	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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Cardiovascular; Neurological/Behavioral; Hepatic/Liver;
Reported Health Effect(s):	Cardiovascular: Heart histopathology and gross pathology; Neurological/Behavioral: Brain histopathology and gross pathology; clinical observations; 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**	

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

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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 Outcome(s):	Skin/Connective Tissue
Reported Health Effect(s):	Skin histopathology and gross pathology
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: Confounding / Variable Control				
	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 Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Mortality
Reported Health Effect(s):	survival
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).
	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 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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	survival
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: Confounding / Variable Control				
	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 — Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Lung, bronchi, trachea 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 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	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				
	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				

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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 Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Lung, bronchi, trachea histopathology and gross pathology
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	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: Confounding / Variable Control				
	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 — Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Testes, prostate, mammary gland, ovary, uterus 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 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	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				
	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				

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Testes, prostate, mammary gland, ovary, uterus histopathology and gross pathology
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	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: Confounding / Variable Control				
	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 Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Thyroid; Immune/Hematological;
Reported Health Effect(s):	Thyroid: Thyroid histopathology and gross pathology; Immune/Hematological: Bone marrow, spleen, lymph nodes, thymus 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 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.
	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 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 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.

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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 Outcome(s):	Thyroid; Immune/Hematological;
Reported Health Effect(s):	Thyroid: Thyroid histopathology and gross pathology; Immune/Hematological: Bone marrow, spleen, lymph nodes, thymus 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 Animals				
	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	Medium	Thyroid: Methodology for the histologic examination was adequately described and addressed the intended outcome.; Immune/Hematological: 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	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: Confounding / Variable Control				
	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	All Outcomes: Incidence data is adequately reported.

Overall Quality Determination — Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Salivary gland, gall bladder, bile duct (mice only), esophagus, stomach, small and large intestine 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 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	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				
	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				

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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 Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Salivary gland, gall bladder, bile duct (mice only), esophagus, stomach, small and large intestine histopathology and gross pathology
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	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: Confounding / Variable Control				
	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 Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	kidney and urinary bladder 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 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	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				
	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				

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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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	kidney and urinary bladder histopathology and gross pathology
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: Confounding / Variable Control				
	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 — Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All tissues were examined for neoplasms
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).
	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 Characterization				
	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				

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All tissues were examined for neoplasms
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	High	Negative control response was adequate.
Domain 6: Confounding / Variable Control				
	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 Uninformative

Study Citation:	NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 66(1978):1-107.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight (6 week and 78 week study), food consumption (78 week study only)
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).
	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				
	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				
	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				

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight (6 week and 78 week study), food consumption (78 week study only)
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: Confounding / Variable Control				
	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 — 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 rats. Toxicology and Applied Pharmacology 28(3):452-464.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Litter effects, embryotoxicity, fetotoxicity
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 Characterization				
	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 (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.

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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):	Reproductive/Developmental
Reported Health Effect(s):	Litter effects, embryotoxicity, fetotoxicity
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				
	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 Assessment				
	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				

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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):	Reproductive/Developmental
Reported Health Effect(s):	Litter effects, embryotoxicity, fetotoxicity
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

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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights and food consumption
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 Characterization				
	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.

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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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights and food consumption
Duration:	Reproductive/Developmental Gestation days 6-15
Chemical:	1,1-Dichloroethane- Parent compound
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 Animals				
	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 Assessment				
	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.
Domain 6: Confounding / Variable Control				
	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).

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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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights and food consumption
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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver weights, gross appearance/pathology and SGPT/ALT activity
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 Characterization				
	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.

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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):	Hepatic/Liver
Reported Health Effect(s):	Liver weights, gross appearance/pathology and SGPT/ALT activity
Duration:	Reproductive/Developmental Gestation days 6-15
Chemical:	1,1-Dichloroethane- Parent compound
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 Animals				
	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 Assessment				
	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 / Variable Control				
	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.

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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):	Hepatic/Liver
Reported Health Effect(s):	Liver weights, gross appearance/pathology and SGPT/ALT activity
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	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

Study Citation:	Dow Chemical, (1947). Results of range-finding toxicological studies on Ethylidene Dichloride.
Health Outcome(s):	Irritation
Reported Health Effect(s):	Skin irritation
Duration:	Not reported "repeated application"
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973137

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Design				
	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				
	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 Animals				
	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.

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Study Citation:	Dow Chemical, (1947). Results of range-finding toxicological studies on Ethylidene Dichloride.
Health Outcome(s):	Irritation
Reported Health Effect(s):	Skin irritation
Duration:	Not reported ”repeated application”
Chemical:	1,1-Dichloroethane- Parent compound
HERO ID:	1973137

Domain	Metric		Rating	Comments
	Metric 18:	Sampling Adequacy	Low	Details of sampling were not reported; this question may be not applicable if a single animal was used.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this study type.
	Metric 20:	Negative Control Response	N/A	Negative control use is not applicable for skin irritation studies.
Domain 6: Confounding / Variable Control				
	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	Statistical methods are not necessary for this study type.
	Metric 24:	Reporting of Data	Low	Signs of irritation were qualitatively reported in the text. No irritation scores were provided.

Overall Quality Determination Uninformative

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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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				
	Metric 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.
	Metric 2:	Test Substance Source	Low	The test substance source was not reported.
	Metric 3:	Test Substance Purity	Low	The test substance purity was not reported.
Domain 2: Test Design				
	Metric 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.
	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 to study groups.
Domain 3: Exposure Characterization				
	Metric 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.
	Metric 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.
	Metric 9:	Reporting of Doses/Concentrations	Medium	A mg/kg dose can be estimated based on the information provided.
	Metric 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.
	Metric 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.
	Metric 12:	Exposure Route and Method	High	The exposure route and method were appropriate for the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	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	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
Duration:	Acute (less than or equal to 24 hr) Single gavage
Chemical:	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.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Body weights were not measured.
	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 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

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 Outcome(s):	Hepatic/Liver; Cardiovascular;
Reported Health Effect(s):	Hepatic/Liver: Nicotinamide coenzymes content in liver; serum ALT and AST, and histopathology; Cardiovascular: Nicotinamide coenzymes content in myocardium and histopathology;
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				
	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				
	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 Characterization				
	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 Animals				
	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.

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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 Outcome(s):	Hepatic/Liver; Cardiovascular;
Reported Health Effect(s):	Hepatic/Liver: Nicotinamide coenzymes content in liver; serum ALT and AST, and histopathology; Cardiovascular: Nicotinamide coenzymes content in myocardium and histopathology;
Duration:	Acute (less than or equal to 24 hr) Single gavage
Chemical:	1,1-Dichloroethane- 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 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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Body weights were not measured.
	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	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 Quality Determination Low

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):	Mortality
Reported Health Effect(s):	Death
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
Domain 1: Test Substance				
	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				
	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 Characterization				
	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.

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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):	Mortality
Reported Health Effect(s):	Death
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 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 Assessment				
	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 Control				
	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.

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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):	Mortality
Reported Health Effect(s):	Death
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	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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Serum ALT, hippuric acid in the urine, and respiration and phosphorylation in liver mitochondria
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
Domain 1: Test Substance				
	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				
	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 Characterization				
	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.

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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):	Hepatic/Liver
Reported Health Effect(s):	Serum ALT, hippuric acid in the urine, and respiration and phosphorylation in liver mitochondria
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
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 Assessment				
	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: Confounding / Variable Control				
	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.

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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):	Hepatic/Liver
Reported Health Effect(s):	Serum ALT, hippuric acid in the urine, and respiration and phosphorylation in liver mitochondria
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 ± m”.

Overall Quality Determination Low

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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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 Substance				
	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 Characterization				
	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 each 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				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
Duration:	Acute (less than or equal to 24 hr) Single gavage
Chemical:	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.
Domain 5: Outcome Assessment				
	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: Confounding / Variable Control				
	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

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 Outcome(s):	Sensitization; Immune/Hematological;
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 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).;
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
Domain 1: Test Substance				
	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				
	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 Characterization				
	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.

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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 Outcome(s):	Sensitization; Immune/Hematological;
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 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).;
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 12:	Exposure Route and Method	High	All Outcomes: The test substance was administered as a single subcutaneous injection.
Domain 4: Test Animals				
	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 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 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.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(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.
Domain 6: Confounding / Variable Control				
	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 measures.
	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	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.

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Health Outcome(s):	Sensitization; Immune/Hematological;
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 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).;
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 Outcome(s):	Immune/Hematological
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 Substance				
	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				
	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 Characterization				
	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 Administration	Low	The gavage volume was not reported.
	Metric 9:	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 Dose/Concentration Spacing	Low	A NOAEL was not obtained. The dose studied was the LD50.
	Metric 12:	Exposure Route and Method	Low	Vehicle not reported.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The source of test animals was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were adequately reported.
	Metric 15:	Number of Animals per Group	Low	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	High	Sampling was adequate (n=6-10).

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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 Outcome(s):	Immune/Hematological
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
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary.
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable 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	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 Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Forestomach cell proliferation
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 Substance				
	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				
	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 Characterization				
	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.

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Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Forestomach cell proliferation
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 Animals				
	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 (forestomach 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: Confounding / Variable Control				
	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 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.); Neurological/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights;
Duration:	Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
HERO ID:	62623

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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 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 dose-response (i.e., both a NOAEL and a LOAEL could not be identified).

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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 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.); Neurological/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights;
Duration:	Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
HERO ID:	62623

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 Animals				
	Metric 13:	Test Animal Characteristics	Low	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; however, they were non-pedigreed and were not likely the best choice for the study.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: No husbandry conditions were not reported; these conditions have the potential to substantially the impact the study results.
	Metric 15:	Number of Animals per Group	Low	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				

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Health Outcome(s):	Immune/Hematological; Hepatic/Liver; Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Mortality; Nutritional/Metabolic;
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Duration:	Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
HERO ID:	62623

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

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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 Outcome(s):	Immune/Hematological; Hepatic/Liver; Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Mortality; Nutritional/Metabolic;
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Duration:	Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
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 mortality (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 not required by study type.; Neurological/Behavioral: Blinding was not required by study type.; Mortality: Blinding was not required by study type. Mortality is not a subjective endpoint.; Nutritional/Metabolic: 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 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.); Neurological/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights;
Duration:	Reproductive/Developmental Approximately 5 months (4 months + gestation) - Dichloroethane
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
HERO ID:	62623

Domain	Metric		Rating	Comments
	Metric 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. Control responses were only 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.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Information on confounding factors (e.g., respiratory rate) were not reported.
	Metric 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.
	Metric 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.

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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 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.); Neurological/Behavioral: Neurological function; Mortality: Spontaneous death; Nutritional/Metabolic: Body weights;
Duration:	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 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).

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.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical signs, conditioned reflex responses, morphological examinations of cerebral cortex
Duration:	Chronic (>91 days) 6-months
Chemical:	1,1-Dichloroethane- Isomer: dichloroethane
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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				
	Metric 7:	Preparation and Storage of Test Substance	Low	No details on the preparation of the test substance or storage conditions were reported.
	Metric 8:	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 concentrations 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.
Domain 4: Test Animals				
	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 Husbandry Conditions	Low	No animal husbandry details were provided.
	Metric 15:	Number of Animals per Group	Low	The number of animals included in the study was not reported.

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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.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical signs, conditioned reflex responses, morphological examinations of cerebral cortex
Duration:	Chronic (>91 days) 6-months
Chemical:	1,1-Dichloroethane- Isomer: dichloroethane
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 5: Outcome 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: Confounding / Variable Control				
	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

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):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Reported Health 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:	Acute (less than or equal to 24 hr) Acute- 4 hour
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200247

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.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				
	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

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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):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Reported Health 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:	Acute (less than or equal to 24 hr) Acute- 4 hour
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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)
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 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).
Domain 6: Confounding / Variable Control				
	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	High	Exposure related to stated outcomes of interest were reported.

Overall Quality Determination Medium

Study Citation:	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.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Clinical chemistry/enzyme activities, histopathology of liver (hepatic steatosis)
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
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The study authors reported using an appropriate concurrent negative control group.
	Metric 2:	Test Substance Source	Low	Manufacturer is reported; however, batch/lot number is not reported.
	Metric 3:	Test Substance Purity	High	Purity not reported, but test substance was analytical grade.
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	A positive control was not included in the study and is not required 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	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.
	Metric 8:	Consistency of Exposure Administration	Low	Gavage dosing volume 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 appropriate for this study type and the outcomes of interest.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	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.
	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 Animals				
	Metric 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.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (including temperature, humidity, light- dark cycle, diet) and were adequate and the same for control and exposed groups.

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Study Citation:	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.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Clinical chemistry/enzyme activities, histopathology of liver (hepatic steatosis)
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 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: Confounding / Variable 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 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

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.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver weight, liver protein, serum AST, ALT, and TG, liver dolichol
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 Substance				
	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				
	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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	The test material was prepared as a solution 50% v/v in mineral oil.
	Metric 8:	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 Animals				
	Metric 13:	Test Animal Characteristics	Medium	Animal age was not reported, only male rats were used.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry was adequately reported
	Metric 15:	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?

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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.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver weight, liver protein, serum AST, ALT, and TG, liver dolichol
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 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
	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 is not necessary for the outcomes evaluated
	Metric 20:	Negative Control Response	High	Negative control responses appeared to be appropriate.
Domain 6: Confounding / Variable 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 (or identified only minor 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 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

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 Outcome(s):	Genotoxicity (Genotoxicity)
Reported Health Effect(s):	In vivo bone marrow micronucleus test
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	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 Characterization				
	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	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				
	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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was reported and scoring method described.

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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 Outcome(s):	Genotoxicity (Genotoxicity)
Reported Health Effect(s):	In vivo bone marrow micronucleus test
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
	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: Confounding / Variable Control				
	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, controlling 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

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 Outcome(s):	Clinical signs (Clinical signs of toxicity)
Reported Health Effect(s):	Acute clinical signs of toxicity: piloerection, hypoactivity, hunched posture, sedation, shallow breathing
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 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	Low	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.
	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 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

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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 Outcome(s):	Clinical signs (Clinical signs of toxicity)
Reported Health Effect(s):	Acute clinical signs of toxicity: piloerection, hypoactivity, hunched posture, sedation, shallow breathing
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 Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology was partially addressed; observations of clinical signs of toxicity
	Metric 17:	Consistency of Outcome Assessment	Low	There was incomplete reporting of details of outcome assessment protocol execution
	Metric 18:	Sampling Adequacy	Medium	5 animals/sex for a preliminary toxicity test; unclear if 5 animals per sex per dose
	Metric 19:	Blinding of Assessors	N/A	Not applicable
	Metric 20:	Negative Control Response	N/A	A negative control was not required
Domain 6: Confounding / Variable Control				
	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 dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure
	Metric 23:	Data Presentation and Analysis	N/A	statistical analysis not necessary; observations of an acute toxicity test; incidence not reported.
	Metric 24:	Reporting of Data	Low	Clinical signs of toxicity were not reported by sex; incidence data were not reported

Overall Quality Determination Uninformative

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 Outcome(s):	Mortality
Reported Health Effect(s):	LD50
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. 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 Characterization				
	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				
	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

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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 Outcome(s):	Mortality
Reported Health Effect(s):	LD50
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 Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology was partially addressed; observations of deaths 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: Confounding / Variable Control				
	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 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	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

Study Citation:	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.
Health Outcome(s):	Mortality; Clinical signs, gross necropsy (Clinical signs, gross necropsy);
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:	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
Domain 1: Test Substance				
	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 Characterization				
	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				

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Study Citation:	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.
Health Outcome(s):	Mortality; Clinical signs, gross necropsy (Clinical signs, gross necropsy);
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:	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
	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: Confounding / Variable Control				
	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 Quality Determination High

Study Citation:	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
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
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 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 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 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				

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Study Citation:	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
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
	Metric 16:	Outcome Assessment Methodology	High	The outcome measurement (body weight) addressed the overall assessment, acute toxicity.
	Metric 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.
	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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Slight body weight changes were measured, although food intake and water consumption was not.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Only a single test group, and no mortality was observed.
	Metric 23:	Data Presentation and Analysis	High	Individual body weight data were provided, and statistical analysis was conducted on the mean.
	Metric 24:	Reporting of Data	High	Individual body weight data were provided along with sex means.

Overall Quality Determination High

Study Citation:	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	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.
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
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 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 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 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				

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Study Citation:	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	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.
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
	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: Confounding / Variable Control				
	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.

Overall Quality Determination High

Study Citation:	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Observations for abnormal urine or feces, abnormalities of the GI tract, excessive soiling
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
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 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 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 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				

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Study Citation:	Dow Chemical, (2005). Ethylene dichloride: Acute vapor inhalation toxicity study in Fischer 344 rats.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Observations for abnormal urine or feces, abnormalities of the GI tract, excessive soiling
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
	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: Confounding / Variable Control				
	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 Quality Determination High

Study Citation:	Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats.
Health Outcome(s):	Mortality; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Mortality (LC50); Nutritional/Metabolic: Body weight;
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 Substance				
	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 Characterization				
	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				

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Study Citation:	Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats.
Health Outcome(s):	Mortality; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Mortality (LC50); Nutritional/Metabolic: Body weight;
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
	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 Assessment				
	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.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Mortality: Not enough information was provided to determine if confounders were 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.

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Study Citation:	Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats.
Health Outcome(s):	Mortality; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Mortality (LC50); Nutritional/Metabolic: Body weight;
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
Overall Quality Determination		**High**	

Study Citation:	Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats.
Health Outcome(s):	Clinical signs, gross necropsy (Clinical signs, gross necropsy)
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:	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 Substance				
	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 Characterization				
	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.

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Study Citation:	Dow Chemical, (2017). [Redacted] 1,2-Dichloroethane: Acute vapor inhalation toxicity study in F344/DuCrl rats.
Health Outcome(s):	Clinical signs, gross necropsy (Clinical signs, gross necropsy)
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:	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
	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 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 / Variable Control				
	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 Quality Determination — High

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.
Health Outcome(s):	Mortality
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 Substance				
	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% pure.
Domain 2: Test Design				
	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 Animals				
	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.

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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.
Health Outcome(s):	Mortality
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 5: Outcome Assessment				
	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 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 (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

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.
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Necropsy with particular attention to the lung
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 Substance				
	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 Design				
	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				
	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 Animals				
	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				

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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.
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Necropsy with particular attention to the lung
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
	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 toxicity 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 was also described in the treated animals. One control animal did not have a catheter present.
Domain 6: Confounding / Variable 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 (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

Study Citation:	Dow Chemical, (1962). Topical application of various solvents and solutions to evaluate dermal irritation.
Health Outcome(s):	Skin/Connective Tissue; Irritation;
Reported Health Effect(s):	Skin/Connective Tissue: Skin irritation; Irritation: Skin irritation;
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
Domain 1: Test Substance				
	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 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 Characterization				
	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.

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Study Citation:	Dow Chemical, (1962). Topical application of various solvents and solutions to evaluate dermal irritation.
Health Outcome(s):	Skin/Connective Tissue; Irritation;
Reported Health Effect(s):	Skin/Connective Tissue: Skin irritation; Irritation: Skin irritation;
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
	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 Animals				
	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 Assessment				
	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: Confounding / Variable Control				
	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).

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Study Citation:	Dow Chemical, (1962). Topical application of various solvents and solutions to evaluate dermal irritation.
Health Outcome(s):	Skin/Connective Tissue; Irritation;
Reported Health Effect(s):	Skin/Connective Tissue: Skin irritation; Irritation: Skin irritation;
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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
Duration:	Acute (less than or equal to 24 hr) Gavage
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	625286

Domain	Metric		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 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				
	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".
Domain 3: Exposure Characterization				
	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 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	The route (gavage) was appropriate for test substance.
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 Assessment				
	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.

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Study Citation:	Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
Duration:	Acute (less than or equal to 24 hr) Gavage
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	625286

Domain	Metric		Rating	Comments
	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 Control				
	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:	Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
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
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 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				
	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 Characterization				
	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. 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				
	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 Assessment				
	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.

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Study Citation:	Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
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 Control				
	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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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
Domain 1: Test Substance				
	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				
	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	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				
	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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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 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 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: Confounding / Variable Control				
	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:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Lung/Respiratory; Nutritional/Metabolic; Lung/Respiratory; 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:	Acute (less 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 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 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:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Lung/Respiratory; Nutritional/Metabolic; Lung/Respiratory; 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:	Acute (less 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
	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 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.
	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				
	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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Lung/Respiratory; Nutritional/Metabolic; Lung/Respiratory; 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:	Acute (less 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
	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 Assessment				
	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 was sensitive and appropriate for the outcomes(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
	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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Lung/Respiratory; Nutritional/Metabolic; Lung/Respiratory; 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:	Acute (less 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
	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 Control				
	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 Quality Determination High

Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: Mortality; Mortality: Mortality;
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
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 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	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 ”counter-balanced 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				
	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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: Mortality; Mortality: Mortality;
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 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	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: Confounding / Variable Control				
	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

Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
Duration:	Acute (less 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 1: Test Substance				
	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				
	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 Animals				
	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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
Duration:	Acute (less 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 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 difficult to interpret
Domain 6: Confounding / Variable Control				
	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 Quality Determination High

Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	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:	Acute (less 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 1: Test Substance				
	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				
	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 Animals				
	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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	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:	Acute (less 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 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: Confounding / Variable Control				
	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 Quality Determination High

Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Hepatic/Liver; Ocular/Sensory;
Reported Health Effect(s):	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.;
Duration:	Acute (less 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 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 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				
	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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Hepatic/Liver; Ocular/Sensory;
Reported Health Effect(s):	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.;
Duration:	Acute (less 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 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: Confounding / Variable Control				
	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 Quality Determination **High**

Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	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:	Acute (less 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 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 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	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 (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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	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:	Acute (less 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
	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				
	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 guideline 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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	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:	Acute (less 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
	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 Control				
	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.

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Study Citation:	Dow Chemical, (2006). Re: Testing consent order for ethylene dichloride; final report (docket no . OPPT-2003-0010).
Health Outcome(s):	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:	Acute (less 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
	Metric 24: Reporting of Data	High	Adrenals (Adrenals): Detailed data tables, figures, and individual animal data were provided.; Necropsy (Gross necropsy of multiple organs and tissues): Detailed data tables, figures, and individual animal data were provided.; Necropsy (Gross necropsy of multiple 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

Study Citation:	Dow Chemical, (1956). Results of skin absorption studies on carbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, and chlorothene.
Health Outcome(s):	Irritation
Reported Health Effect(s):	Irritation, corrosion and damage to the skin were assessed.
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
Domain 1: Test Substance				
	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 3: Exposure Characterization				
	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				
	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 Assessment				

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Study Citation:	Dow Chemical, (1956). Results of skin absorption studies on carbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, and chlorothene.
Health Outcome(s):	Irritation
Reported Health Effect(s):	Irritation, corrosion and damage to the skin were assessed.
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 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
Domain 6: Confounding / Variable Control				
	Metric 21:	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	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 Quality Determination Low

Study Citation:	Dow Chemical, (1956). Results of skin absorption studies on carbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, and chlorothene.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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
Domain 1: Test Substance				
	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 Characterization				
	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				
	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 Assessment				
	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.

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Study Citation:	Dow Chemical, (1956). Results of skin absorption studies on carbon tetrachloride, ethylene dichloride, tetrachloroethylene, trichloroethylene, and chlorothene.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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 / Variable Control				
	Metric 21:	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

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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality 24 and 48 hours after exposure.
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 Substance				
	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 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 Animals				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality 24 and 48 hours after exposure.
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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant and therefore respiratory rate should be reported.
	Metric 22:	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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Relative kidney weight and renal tubular damage (histopathology)
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 Substance				
	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 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 Animals				
	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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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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Relative kidney weight and renal tubular damage (histopathology)
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 Assessment				
	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 regarding outcomes assessment protocol were minimal, but unlikely to substantially impact results.
	Metric 18:	Sampling Adequacy	High	The sampling was adequate. Renal pathology: n=4-5; Relative Kidney weight: n=5
	Metric 19:	Blinding of Assessors	N/A	Blinding was not needed.
	Metric 20:	Negative Control Response	Low	Negative control data was not reported for kidney histology.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant 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 differences unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described and appropriate.
	Metric 24:	Reporting of Data	High	Data on exposure related outcomes were reported for kidney.

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Relative liver weight
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 Substance				
	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 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	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 Animals				
	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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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Relative liver weight
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 Assessment				
	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: Confounding / Variable Control				
	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 differences 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

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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Water content of cortex and medulla; brain neurotransmitter levels
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 1: Test Substance				
	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				
	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 Characterization				
	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 Animals				
	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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Water content of cortex and medulla; brain neurotransmitter levels
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 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 neurotransmitters 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: Confounding / Variable Control				
	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**

Study Citation:	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.
Health Outcome(s):	Neurological/Behavioral; Gastrointestinal; Musculoskeletal;
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs; Gastrointestinal: Diarrhea, necropsy findings; Musculoskeletal: Muscle weakness;
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.
	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: Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile)
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: No information is provided on gavage volume.
	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 Dose/Concentration Spacing	High	All Outcomes: 5 doses and the spacing was adequate to detect a range of responses.
	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 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 Assessment				

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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 Outcome(s):	Neurological/Behavioral; Gastrointestinal; Musculoskeletal;
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs; Gastrointestinal: Diarrhea, necropsy findings; Musculoskeletal: Muscle weakness;
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	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).
	Metric 19:	Blinding of Assessors	Low	All Outcomes: Blinding was not reported and assessment of clinical signs may be affected by knowledge of dose group.
	Metric 20:	Negative Control Response	N/A	All Outcomes: Negative controls were not used.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: 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	Neurological/Behavioral: Clinical signs were described in text only.; Gastrointestinal: Clinical signs and necropsy results were described in text only.; Musculoskeletal: Data for exposure-related findings were not shown for each study group, but results were described in the text.

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 Outcome(s):	Ocular/Sensory; Cardiovascular; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Lung/Respiratory;
Reported Health Effect(s):	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;
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.
	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: Information on preparation and storage was not reported and lack of details could substantially impact results (substance is volatile)
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: No information is provided on gavage volume.
	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 Dose/Concentration Spacing	High	All Outcomes: 5 doses and the spacing was adequate to detect a range of responses.
	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 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 Assessment				

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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 Outcome(s):	Ocular/Sensory; Cardiovascular; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Lung/Respiratory;
Reported Health Effect(s):	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;
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 further 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 weight 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.; 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., were all animals necropsied?).; Nutritional/Metabolic: Details regarding sampling were not reported (i.e., was body weight measured for all animals?).; Hepatic/Liver: Details regarding sampling were not reported (i.e., were all animals necropsied?).; Renal/Kidney: 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: Blinding 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/Kidney: 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

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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 Outcome(s):	Ocular/Sensory; Cardiovascular; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Lung/Respiratory;
Reported Health Effect(s):	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;
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

Study Citation:	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Decreased body weight
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 1: Test Substance				
	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 Characterization				
	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				
	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 Assessment				
	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.
	Metric 20:	Negative Control Response	N/A	Negative controls were not used.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Decreased body weight
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

Study Citation:	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Deaths
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 1: Test Substance				
	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 Characterization				
	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				
	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 Assessment				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Deaths
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: Confounding / Variable Control				
	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	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 Outcome(s):	Irritation
Reported Health Effect(s):	Gastrointestinal (oral), skin (dermal)
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 1: Test Substance				
	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 Characterization				
	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				
	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 Assessment				
	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.
	Metric 17:	Consistency of Outcome Assessment	Low	Outcome assessment details were not provided (i.e., timing/frequency skin was examined for evidence of irritation).
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling were not reported.

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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 Outcome(s):	Irritation
Reported Health Effect(s):	Gastrointestinal (oral), skin (dermal)
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: Confounding / Variable Control				
	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 Uninformative

Study Citation:	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.
Health Outcome(s):	Lung/Respiratory
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
Domain 1: Test Substance				
	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 Characterization				
	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				
	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 Assessment				
	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).

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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 Outcome(s):	Lung/Respiratory
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: Confounding / Variable Control				
	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	Uninformative	The report does not differentiate among findings in multiple exposure groups.

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 Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Diarrhea, 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
Domain 1: Test Substance				
	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 Characterization				
	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				
	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 Assessment				
	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.

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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 Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Diarrhea, 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 20:	Negative Control Response	N/A	Negative controls were not used.
Domain 6: Confounding / Variable Control				
	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	Low	Clinical signs were 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 Outcome(s):	Mortality
Reported Health Effect(s):	Deaths
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	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				
	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 Characterization				
	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 Administration	Low	No information is provided on gavage volume.
	Metric 9:	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 Dose/Concentration Spacing	High	5 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				
	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 1 animals/group was used.
Domain 5: Outcome Assessment				
	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	Negative controls were not used.
Domain 6: Confounding / Variable Control				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Deaths
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	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 (1 rabbit/group)
	Metric 24:	Reporting of Data	High	Mortality data were provided for each group/animal.

Overall Quality Determination Uninformative

Study Citation:	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 Outcome(s):	Hepatic/Liver; Genotox (Genotox); Mortality;
Reported Health Effect(s):	Hepatic/Liver: Serum ALT activity, hepatic ornithine decarboxylase activity and cytochrome P-450 content; Genotox (Genotox): Hepatic DNA damage (by alkaline elution); Mortality: Mortality.;
Duration:	Acute (less than or equal to 24 hr) 21 hours
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	6118

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 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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: 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	All Outcomes: Test substance was administered consistently across study groups
	Metric 9:	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 before sacrifice).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Only one dose was studied. This dose was chosen based on either LD50 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 Animals				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: All relevant animal characteristics were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Rats were caged 3 per cage and provided food and water ad libitum. 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.
Domain 5: Outcome Assessment				
	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.

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Study Citation:	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 Outcome(s):	Hepatic/Liver; Genotox (Genotox); Mortality;
Reported Health Effect(s):	Hepatic/Liver: Serum ALT activity, hepatic ornithine decarboxylase activity and cytochrome P-450 content; Genotox (Genotox): Hepatic DNA damage (by alkaline elution); Mortality: Mortality.;
Duration:	Acute (less than or equal to 24 hr) 21 hours
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	6118

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: Confounding / Variable Control				
	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.

Overall Quality Determination High

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 Outcome(s):	Skin/Connective Tissue
Reported Health Effect(s):	Localized microscopic examinations of the skin (at the application site)
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
Domain 1: Test Substance				
	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				
	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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	The test substance was applied undiluted; no preparation was necessary. It was not specified 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				
	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.

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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 Outcome(s):	Skin/Connective Tissue
Reported Health Effect(s):	Localized microscopic examinations of the skin (at the application site)
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 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: Confounding / Variable Control				
	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 Uninformative

Study Citation:	Livesey, J. C. (1982). Studies on the metabolism and toxicity of 1,2-dihaloethanes.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: BUN, serum creatinine levelsUrine was collected and analyzed for LDH, alkaline phophatase, g-glutamyl transpeptidase, urine flow rate 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 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 Characterization				
	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				
	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 Assessment				
	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.

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Study Citation:	Livesey, J. C. (1982). Studies on the metabolism and toxicity of 1,2-dihaloethanes.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: BUN, serum creatinine levelsUrine was collected and analyzed for LDH, alkaline phophatase, g-glutamyl transpeptidase, urine flow rate 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: Confounding / Variable Control			
	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).

Overall Quality Determination High

Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Nutritional/Metabolic; Lung/Respiratory; Mortality; Hepatic/Liver;
Reported Health Effect(s):	Nutritional/Metabolic: Weight change; Lung/Respiratory: Gross pathology; Mortality: Death (LD50); Hepatic/Liver: Gross pathology;
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 Substance				
	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				
	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				

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Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Nutritional/Metabolic; Lung/Respiratory; Mortality; Hepatic/Liver;
Reported Health Effect(s):	Nutritional/Metabolic: Weight change; Lung/Respiratory: Gross pathology; Mortality: Death (LD50); Hepatic/Liver: Gross pathology;
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 Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not reported.
	Metric 15:	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 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: Confounding / Variable Control				
	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	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 Uninformative

Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Death (LD50)
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 Substance				
	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 Design				
	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 Animals				
	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				

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Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Death (LD50)
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 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 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 (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 Uninformative

Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Renal/Kidney: Gross Pathology; Hepatic/Liver: Gross pathology; Lung/Respiratory: Gross pathology; Gastrointestinal: Gross pathology;
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 Substance				
	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				
	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	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 dose groups; Gastrointestinal: 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
	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 Animals				
	Metric 13:	Test Animal Characteristics	Low	All Outcomes: Minimal details on test animals were provided. - species and sex only

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Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Renal/Kidney: Gross Pathology; Hepatic/Liver: Gross pathology; Lung/Respiratory: Gross pathology; Gastrointestinal: Gross pathology;
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 Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not reported.
	Metric 15:	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 Assessment				
	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 / Variable Control				
	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	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 Uninformative

Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Death (LD50)
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 1: Test Substance				
	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 Design				
	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	Substance administered undiluted. Storage was not reported.
	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
	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 Animals				
	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.

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Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Death (LD50)
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 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 (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 Uninformative

Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Weight change
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 1: Test Substance				
	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 Design				
	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	Substance administered undiluted. Storage was not reported.
	Metric 8:	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 Dose/Concentration Spacing	High	Study included 4 dose groups
	Metric 12:	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.
Domain 4: Test Animals				
	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				
	Metric 16:	Outcome Assessment Methodology	High	Body weights were measured on day 14 for surviving animals

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Study Citation:	Mellon Institute of Industrial Research, (1948). The toxicity of ethylene dichloride.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Weight change
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
	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 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 (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 Uninformative

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (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
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	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 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	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.
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 Assessment				
	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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (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 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: Confounding / Variable Control				
	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.

Overall Quality Determination 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 Outcome(s):	Nutritional/Metabolic
Reported Health 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
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 body 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	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 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 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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health 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 / Variable Control				
	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 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

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Decreased absolute liver weight (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
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 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	A single gavage dose is appropriate for 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 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 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.

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Decreased absolute liver weight (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
Domain 6: Confounding / Variable Control			
	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

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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
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
Domain 1: Test Substance				
	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 Characterization				
	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.

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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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
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 Assessment				
	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: Confounding / Variable 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 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 with alkyl halides and other hepatotoxins. Molecular Pharmacology 20(3):685-693.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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
Domain 1: Test Substance				
	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 Characterization				
	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.

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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):	Mortality
Reported Health Effect(s):	Survival
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 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: Confounding / Variable 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 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):	Hepatic/Liver
Reported Health Effect(s):	Systemic: Relative liver weightsMechanistic: measurements of microsomal total protein, RNA content, phospholipids, and diene conjugates. Cytochrome P-450 content, NADPH cytochrome reductase, and cytochrome B5 content were also measured along with the relative content of fatty acids from lipid extracts and measurements of linoleic and arachidonic acid.
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
Domain 1: Test Substance				
	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 Characterization				
	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.

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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):	Hepatic/Liver
Reported Health Effect(s):	Systemic: Relative liver weightsMechanistic: measurements of microsomal total protein, RNA content, phospholipids, and diene conjugates. Cytochrome P-450 content, NADPH cytochrome reductase, and cytochrome B5 content were also measured along with the relative content of fatty acids from lipid extracts and measurements of linoleic and arachidonic acid.
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 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 endpoints 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: Confounding / Variable 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 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.

Overall Quality Determination Medium

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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Immunohistochemistry to assess damage of renal proximal tubules
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
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 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 Characterization				
	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 Administration	Low	Gavage volume was not reported.
	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 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 Husbandry Conditions	Medium	Not all husbandry conditions were fully reported. Study states animals were under controlled 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 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	High	Sampling was adequate.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary.

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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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Immunohistochemistry to assess damage of renal proximal tubules
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: Confounding / Variable 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	High	Data were fully reported.

Overall Quality Determination High

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 Outcome(s):	Mortality
Reported Health Effect(s):	LD50
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 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
	Metric 3:	Test Substance Purity	Low	Not reported
Domain 2: Test Design				
	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 Characterization				
	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 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
	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 Assessment				
	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

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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 Outcome(s):	Mortality
Reported Health Effect(s):	LD50
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
	Metric 20:	Negative Control Response	N/A	not necessary
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	there were not reported differences among 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
	Metric 23:	Data Presentation and Analysis	High	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

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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary glucose and protein; renal histopathology
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				
	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 Characterization				
	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 Dose/Concentration Spacing	Medium	There were minor limitation in dose 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 Husbandry Conditions	Low	Husbandry conditions were not reported.
	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 Assessment				
	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.

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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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary glucose and protein; renal histopathology
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 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 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 Pharmacology 7(1):37-44.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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				
	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				
	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 Characterization				
	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 Dose/Concentration Spacing	Medium	There were minor limitation in dose 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 Husbandry Conditions	Low	Husbandry conditions were not reported.
	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 Assessment				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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: 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 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

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 Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Biochemical and histological changes in lung, relative lung weight; includes mechanistic endpoints
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
Domain 1: Test Substance				
	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 Characterization				
	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				
	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 Assessment				

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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 Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Biochemical and histological changes in lung, relative lung weight; includes mechanistic endpoints
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 ho-mogenate assessment; Histological outcomes for controls were not reported.
Domain 6: Confounding / Variable Control				
	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 eval-uation 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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge
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 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
	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	preparation of the test substance was reported and appropriate. storage was not reported
	Metric 8:	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 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 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 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.

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge
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
	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: Confounding / Variable Control				
	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

Overall Quality Determination High

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 Outcome(s):	Immune/Hematological; Immune/Hematological;
Reported Health Effect(s):	Immune/Hematological: lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge; Immune/Hematological: lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge;
Duration:	Acute (less than or equal to 24 hr) 3h-single dose rat
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	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				
	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 Characterization				
	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 Animals				
	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 groups.
	Metric 15:	Number of Animals per Group	Low	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 Assessment				

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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 Outcome(s):	Immune/Hematological; Immune/Hematological;
Reported Health Effect(s):	Immune/Hematological: lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge; Immune/Hematological: lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge;
Duration:	Acute (less than or equal to 24 hr) 3h-single dose rat
Chemical:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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 Quality Determination 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 Outcome(s):	Nutritional/Metabolic
Reported Health 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 Substance				
	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 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 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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health 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 4: Test Animals				
	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 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: Confounding / Variable Control				
	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 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

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 Outcome(s):	Mortality
Reported Health Effect(s):	Death
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 Substance				
	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 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 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 (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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Death
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 specified, 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 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: Confounding / Variable Control				
	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 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**

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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical 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
Domain 1: Test Substance				
	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 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 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				

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical 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
	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 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 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 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 18:	Sampling Adequacy	High	All animals were observed
	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 and Procedures	Medium	No confounding variables were reported.
	Metric 22:	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 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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical 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
	Metric 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

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 Outcome(s):	Immune/Hematological; Hepatic/Liver; Lung/Respiratory; Endocrine (Endocrine); Renal/Kidney;
Reported Health Effect(s):	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 (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

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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	N/A	All Outcomes: Not necessary for acute lethality studies
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for acute toxicity studies
	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
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.
	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.

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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 Outcome(s):	Immune/Hematological; Hepatic/Liver; Lung/Respiratory; Endocrine (Endocrine); Renal/Kidney;
Reported Health Effect(s):	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 (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

Domain	Metric		Rating	Comments
Domain 4: Test Animals				
	Metric 13:	Test 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 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry information was limited to the diets provided. No other data were provided.
	Metric 15:	Number 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 Assessment				
	Metric 16:	Outcome 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 17:	Consistency of Outcome Assessment	Low	All Outcomes: Details of the consistency the of outcome assessment were not 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 this study type
	Metric 20:	Negative 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

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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 Outcome(s):	Immune/Hematological; Hepatic/Liver; Lung/Respiratory; Endocrine (Endocrine); Renal/Kidney;
Reported Health Effect(s):	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 (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

Domain	Metric		Rating	Comments
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.
	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.
	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

Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.
Health Outcome(s):	Mortality
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
Domain 1: Test Substance				
	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				
	Metric 4:	Negative and Vehicle Controls	N/A	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 Administration	Low	Gavage volumes were not reported.
	Metric 9:	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 Animals				
	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				

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Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.
Health Outcome(s):	Mortality
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 Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	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.
	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 Outcome(s):	Missing 'other' target organ
Reported Health Effect(s):	Gross pathology - no specific methods reported
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				
	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				
	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 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 Administration	Low	Gavage volumes were not reported.
	Metric 9:	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 Animals				
	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 for gross pathological observation was not clearly reported.
	Metric 17:	Consistency of Outcome Assessment	High	The outcomes were assessed consistently across study groups.

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Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.
Health Outcome(s):	Missing 'other' target organ
Reported Health Effect(s):	Gross pathology - no specific methods reported
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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	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.
	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

Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Signs of depression and ataxia
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				
	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				
	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 Administration	Low	Gavage volumes were not reported.
	Metric 9:	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 Animals				
	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.

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Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Signs of depression and ataxia
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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	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.
	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:	Storer, R. D., Conolly, R. B. (1983). Comparative in vivo genotoxicity and acute hepatotoxicity of three 1,2-dihaloethanes. Carcinogenesis 4(11):1491-1494.
Health Outcome(s):	In vivo genotoxicity (In vivo genotoxicity)
Reported Health Effect(s):	In vivo genotoxicity (DNA damage) in hepatic tissue
Duration:	Acute (less than or equal to 24 hr) In vivo genotoxicity
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5549990

Domain	Metric		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	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 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 Dose/Concentration Spacing	High	Then number of exposure groups and doses were adequate to elicit full range of responses.
	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 Husbandry Conditions	Medium	Husbandry conditions were not sufficiently reported, but unlikely to have substantial impacts.
	Metric 15:	Number of Animals per Group	Medium	Only 6 animals per group were used.
Domain 5: Outcome Assessment				
	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 18:	Sampling Adequacy	High	Sampling was adequate for outcomes of interest.

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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.
Health Outcome(s):	In vivo genotoxicity (In vivo genotoxicity)
Reported Health Effect(s):	In vivo genotoxicity (DNA damage) in hepatic tissue
Duration:	Acute (less than or equal to 24 hr) In vivo genotoxicity
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5549990

Domain	Metric		Rating	Comments
	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.
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	High	Exposure related outcomes were reported.

Overall Quality Determination High

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.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Relative liver weight, serum levels of L-iditol dehydrogenase (SDH) and alanine aminotransferase (AAT or ALT)
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 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 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 Dose/Concentration Spacing	High	Then number of exposure groups and doses were adequate to elicit full range of responses.
	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 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 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.
	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.

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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.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Relative liver weight, serum levels of L-iditol dehydrogenase (SDH) and alanine aminotransferase (AAT or ALT)
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

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.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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 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 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 Dose/Concentration Spacing	Medium	Minor limitations (full range of responses was not obtained)
	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 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 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.

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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.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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 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

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.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Relative kidney weight and blood urea level (BUN)
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 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 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 Dose/Concentration Spacing	Medium	Minor limitations (full range of responses was not obtained) for renal (BUN).
	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 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 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.
	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.

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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.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Relative kidney weight and blood urea level (BUN)
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

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 Outcome(s):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: Kidney weight; Hepatic/Liver: Liver weight, serum IDH (L-iditol (also called sorbitol) dehydrogenase), and alanine aminotransferase;
Duration:	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				
	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%
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 Characterization				
	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 endpoints reported.; Hepatic/Liver: The exposure route was generally appropriate for evaluating the acute endpoints reported
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Animal species, strain, sex, age, and source were reported. Starting body weights were not provided.

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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 Outcome(s):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: Kidney weight; Hepatic/Liver: Liver weight, serum IDH (L-iditol (also called sorbitol) dehydrogenase), and alanine aminotransferase;
Duration:	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
	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 Assessment				
	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: Confounding / Variable Control				
	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 Quality Determination 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 Outcome(s):	in vivo genotoxcity (in vivo genotoxicity)
Reported Health Effect(s):	Double-stranded DNA breaks in hepatic DNA from mice treated in vivo.
Duration:	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				
	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				
	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 Characterization				
	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 significantly 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				
	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.

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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 Outcome(s):	in vivo genotoxcity (in vivo genotoxicity)
Reported Health Effect(s):	Double-stranded DNA breaks in hepatic DNA from mice treated in vivo.
Duration:	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
	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 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: Confounding / Variable 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 (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 Quality Determination High

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 Effect(s):	in vivo genotoxicity (Genotoxicity): Hepatic DNA damage; in vivo genotoxicity (Genotoxicity): Hepatic DNA damage;
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 Substance				
	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				
	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 Characterization				
	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 Administration	High	All Outcomes: 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	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				

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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 Outcome(s):	in vivo genotoxicity (Genotoxicity); in vivo genotoxicity (Genotoxicity);
Reported Health Effect(s):	in vivo genotoxicity (Genotoxicity): Hepatic DNA damage; in vivo genotoxicity (Genotoxicity): Hepatic DNA damage;
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 Assessment				
	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: Confounding / Variable Control				
	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 Quality Determination			**High**	

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)
Reported Health Effect(s):	Hepatic DNA damage
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 Substance				
	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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Details of inhalation chamber preparation were limited.
	Metric 8:	Consistency of Exposure Administration	High	Exposure administration was consistent across groups.
	Metric 9:	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 Dose/Concentration Spacing	High	Number of exposure groups was adequate and spacing covered the range of effect.
	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 Assessment				
	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.
	Metric 19:	Blinding of Assessors	N/A	Not necessary.
	Metric 20:	Negative Control Response	High	Negative controls responded appropriately.

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Health Outcome(s):	in vivo genotoxicity (Genotoxicity)
Reported Health Effect(s):	Hepatic DNA damage
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 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	High mortality was observed at high doses where DNA damage was observed, but lower 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

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Health Outcome(s):	Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Hepatic/Liver: liver weight, clinical chem, hepatic DNA damage; Renal/Kidney: kidney weight, clinical chem;
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 Substance				
	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				
	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 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	All Outcomes: The number of animals was sufficient for the study type and outcome.
Domain 5: Outcome Assessment				

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Health Outcome(s):	Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Hepatic/Liver: liver weight, clinical chem, hepatic DNA damage; Renal/Kidney: kidney weight, clinical chem;
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 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 Control				
	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	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

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):	Mortality
Reported Health Effect(s):	death
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 Substance				
	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				
	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	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 Administration	High	Exposure administration was consistent across groups.
	Metric 9:	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 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 was sufficient for the study type and outcome.
Domain 5: Outcome 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.
	Metric 19:	Blinding of Assessors	N/A	Not necessary.
	Metric 20:	Negative Control Response	High	Negative controls responded appropriately.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	death
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 6: Confounding / Variable Control				
	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.

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-dichloroethane in mice: Comparison of oral, intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.
Health Outcome(s):	Mortality
Reported Health Effect(s):	death
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 1: Test Substance				
	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	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 Administration	High	Exposure administration was consistent across groups.
	Metric 9:	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	High	Number of exposure groups and spacing was adequate
	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 was sufficient for the study type and outcome.
Domain 5: Outcome 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.

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Health Outcome(s):	Mortality
Reported Health Effect(s):	death
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 / Variable Control			
	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 across 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.

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-dichloroethane in mice: Comparison of oral, intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: kidney weight, clinical chem; Hepatic/Liver: liver weight, clinical chem, hepatic DNA damage;
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 1: Test Substance				
	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				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Vehicle control was appropriate.
	Metric 5:	Positive Controls	N/A	Renal/Kidney: Not necessary for the study type.; Hepatic/Liver: ccl4 was used as a positive control for liver
	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	Medium	All Outcomes: 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 Administration	High	All Outcomes: 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	Renal/Kidney: Single administration is appropriate.; Hepatic/Liver: A single administration is appropriate for evaluation of acute effects.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Renal/Kidney: Number of exposure groups was adequate and spacing covered the range of effect.; Hepatic/Liver: The number of exposure groups was adequate and spacing covered the range of effect.
	Metric 12:	Exposure Route and Method	High	Renal/Kidney: Route was suited to the test substance.; Hepatic/Liver: The route was suited to the test substance.
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	All Outcomes: Number of animals was sufficient for the study type and outcome.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Outcome assessment methodology partially addressed the outcome.

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Health Outcome(s):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: kidney weight, clinical chem; Hepatic/Liver: liver weight, clinical chem, hepatic DNA damage;
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: Confounding / Variable Control				
	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	All Outcomes: 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	All Outcomes: 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-dichloroethane in mice: Comparison of oral, intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.
Health Outcome(s):	Mortality; Renal/Kidney;
Reported Health Effect(s):	Mortality: death; Renal/Kidney: kidney weight, clinical chem;
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 Substance				
	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				
	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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Details of inhalation chamber preparation were limited.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: 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	Mortality: A single 4h exposure was appropriate; Renal/Kidney: A single 4 h 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.
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.
Domain 5: Outcome Assessment				
	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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Health Outcome(s):	Mortality; Renal/Kidney;
Reported Health Effect(s):	Mortality: death; Renal/Kidney: kidney weight, clinical chem;
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: Confounding / Variable Control				
	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.

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-dichloroethane in mice: Comparison of oral, intraperitoneal, and inhalation routes of exposure. Cancer Research 44(10):4267-4271.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver weight, clinical chem, hepatic DNA damage
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 Substance				
	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.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Details of inhalation chamber preparation were limited.
	Metric 8:	Consistency of Exposure Administration	Medium	Exposure administration was consistent across groups, control was room air.
	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 Dose/Concentration Spacing	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:	Exposure Route and Method	High	The 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. Animcals 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	The number of animals was sufficient for the study type and outcome.
Domain 5: Outcome Assessment				
	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

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver weight, clinical chem, hepatic DNA damage
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 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	Statistics were reported and appropriate.
	Metric 24:	Reporting of Data	High	Data were reported for all groups.

Overall Quality Determination High

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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Righting reflex test, Bridge test, FR20 operant test and MULT operant test
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
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 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 Characterization				
	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 Animals				
	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 Assessment				
	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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Righting reflex test, Bridge test, FR20 operant test and MULT operant test
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
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	High	Negative control group responses were appropriate.
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	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

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 Outcome(s):	Mortality
Reported Health Effect(s):	24 hour lethality
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
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 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	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.
Domain 3: Exposure Characterization				
	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 Animals				
	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 Assessment				
	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.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	N/A	Negative control group was not studied.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	24 hour lethality
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
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	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

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 Outcome(s):	Mortality; Neurological/Behavioral;
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 mortalityrates 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
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/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				
	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 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 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.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Only one concentration was studied; concentration was justified based on effects in previous findings.
	Metric 12:	Exposure Route and Method	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 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 (n=6).
Domain 5: Outcome Assessment				

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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 Outcome(s):	Mortality; Neurological/Behavioral;
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 mortalityrates 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 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodology were appropriate
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: 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: Confounding / Variable Control				
	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	Mortality: Mortality data are reported for all groups but data on poisoned symptoms are not adequately reported.; Neurological/Behavioral: Data were adequately reported.

Overall Quality Determination — Uninformative

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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: mortality; Mortality: mortality;
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 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. 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				
	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 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	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 Dose/Concentration Spacing	Medium	All Outcomes: Number of exposure groups/spacing were adequate.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The number of air changes/hour were not reported.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age of animals 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/group was acceptable.
Domain 5: Outcome 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.

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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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: mortality; Mortality: mortality;
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
	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.
Domain 6: Confounding / Variable 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	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 Outcome(s):	Neurological/Behavioral; Neurological/Behavioral;
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 1: Test Substance				
	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				
	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 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	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 Dose/Concentration Spacing	Medium	All Outcomes: Number of exposure groups/spacing were adequate.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The number of air changes/hour were not reported.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age of animals 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/group was acceptable.
Domain 5: Outcome Assessment				
	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.

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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 Outcome(s):	Neurological/Behavioral; Neurological/Behavioral;
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 / Variable 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

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):	Neurological/Behavioral; Neurological/Behavioral;
Reported Health Effect(s):	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.;
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

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 1 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 specific neurological endpoints evaluated.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Study authors stated 'animals were randomly divided' to dose groups.
Domain 3: Exposure Characterization				

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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):	Neurological/Behavioral; Neurological/Behavioral;
Reported Health Effect(s):	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.;
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

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 Animals				
	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				

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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):	Neurological/Behavioral; Neurological/Behavioral;
Reported Health Effect(s):	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.;
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

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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: No differences explicitly reported among study groups.Test substance is a respiratory irritant (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 Exposure	Medium	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 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.

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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):	Neurological/Behavioral; Neurological/Behavioral;
Reported Health Effect(s):	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.;
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

Domain	Metric		Rating	Comments
	Metric 23:	Data Presentation and Analysis	High	Neurological/Behavioral: Seemed acceptable with pair-wise comparison analyses performed.; Neurological/Behavioral: Seemed acceptable with pair-wise comparison analyses 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 histopathological findings.

Overall Quality Determination Uninformative

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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Developmental
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
Domain 1: Test Substance				
	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				
	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 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.
	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.
	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.

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Developmental
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 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 inconsistencies 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: Confounding / Variable Control				
	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

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 Outcome(s):	Neurological/Behavioral; Neurological/Behavioral;
Reported Health Effect(s):	Neurological/Behavioral: Animal behavior/activity; diffusion magnetic resonance imaging on brains, histology on brains and acute 1,2-DCE-induced toxicencephalopathy.; Neurological/Behavioral: Animal behavior/activity; diffusion magnetic resonance imaging on brains, histology on brains and acute 1,2-DCE-induced toxicencephalopathy.;
Duration:	Acute (less than or equal to 24 hr) 1.5 hours
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4697102

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 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 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 Administration	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	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.

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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 toxic encephalopathy in rats. In Vivo 30(6):787-793.
Health Outcome(s):	Neurological/Behavioral; Neurological/Behavioral;
Reported Health Effect(s):	Neurological/Behavioral: Animal behavior/activity; diffusion magnetic resonance imaging on brains, histology on brains and acute 1,2-DCE-induced toxicencephalopathy.; Neurological/Behavioral: Animal behavior/activity; diffusion magnetic resonance imaging on brains, histology on brains and acute 1,2-DCE-induced toxicencephalopathy.;
Duration:	Acute (less than or equal to 24 hr) 1.5 hours
Chemical:	1,1-Dichloroethane- 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 Assessment				
	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: Confounding / Variable Control				
	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	All Outcomes: Histology was not shown for all groups.

Overall Quality Determination **Medium**

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):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Reported Health 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:	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
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.

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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):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Reported Health 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:	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
	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)."
Domain 6: Confounding / Variable Control				
	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).

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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):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Reported Health 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:	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.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight gain
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 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 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 Administration	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 and Dose/Concentration Spacing	High	The number of dose groups was adequate and justified based on LD50.
	Metric 12:	Exposure Route and Method	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 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Water availability was not reported.
	Metric 15:	Number of Animals per Group	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 17:	Consistency of Outcome Assessment	Medium	There was no information provided as to when or how often body weight was assessed. This is unlikely to substantially impact results.
	Metric 18:	Sampling Adequacy	Low	It is not clear how many animals were evaluated.

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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.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight gain
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 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 / Variable Control				
	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

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.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Neurological/Behavioral;
Reported Health Effect(s):	Renal/Kidney: Gross examination of kidney; Hepatic/Liver: Gross examination of 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 Substance				
	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				
	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				
	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 Administration	High	All Outcomes: Test substance was administered consistently across study groups.
	Metric 9:	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 Dose/Concentration Spacing	High	All Outcomes: The number of dose groups was adequate and justified based on LD50.
	Metric 12:	Exposure Route and Method	High	All Outcomes: Route of exposure (i.p. injection) was adequate.
Domain 4: Test Animals				
	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				

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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.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Neurological/Behavioral;
Reported Health Effect(s):	Renal/Kidney: Gross examination of kidney; Hepatic/Liver: Gross examination of 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
	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: Confounding / Variable Control				
	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

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.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Male fertility, histopathology of testis
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 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 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 Administration	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 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 Animals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Water availability was not reported.
	Metric 15:	Number of Animals per Group	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 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.

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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.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Male fertility, histopathology of testis
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: Confounding / Variable Control				
	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

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.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Male fertility, histopathology of testis
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 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 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 Administration	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 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.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Water availability was not reported.
	Metric 15:	Number of Animals per Group	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 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.
	Metric 20:	Negative Control Response	High	Negative control response was appropriate.

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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.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Male fertility, histopathology of testis
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: Confounding / Variable Control				
	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.

Overall Quality Determination — High

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):	Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/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;
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	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.

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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):	Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/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;
Duration:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62965

Domain	Metric		Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	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.; Nutritional/Metabolic: 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.

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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):	Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/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;
Duration:	Short-term (>1-30 days) 10 days
Chemical:	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	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, 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.

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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):	Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/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;
Duration:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62965

Domain	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.

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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):	Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/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;
Duration:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	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.; Lung/Respiratory: 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.
Domain 6: Confounding / Variable Control				
	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.

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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):	Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/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;
Duration:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62965

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 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, and water consumption.

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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):	Renal/Kidney; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Mortality; Cardiovascular; Reproductive/Developmental; Immune/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;
Duration:	Short-term (>1-30 days) 10 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62965

Domain	Metric	Rating	Comments
	Metric 24: Reporting of Data	High	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, histopathology) or quantitatively (organ weight).; Neurological/Behavioral: Negative findings were reported qualitatively (gross pathology, histopathology) or quantitatively (brain weight).; Nutritional/Metabolic: All data were reported adequately. Negative findings were reported qualitatively (food and water consumption) or quantitatively (body weight).

Overall Quality Determination High

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):	Hepatic/Liver
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:	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 Substance	High	The test substance is volatile and was mixed fresh daily.
	Metric 8:	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 highest dose, 300 mg/kg/day, was chosen because it was approximately 44% 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 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.
Domain 5: Outcome Assessment				

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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):	Hepatic/Liver
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:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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.

Overall Quality Determination High

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):	Ocular/Sensory; Thyroid; Musculoskeletal; Skin/Connective Tissue;
Reported Health Effect(s):	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
HERO ID:	62965

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.

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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):	Ocular/Sensory; Thyroid; Musculoskeletal; Skin/Connective Tissue;
Reported Health Effect(s):	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
HERO ID:	62965

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, which is standard practice.
	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.
Domain 6: Confounding / Variable Control				
	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.

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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):	Ocular/Sensory; Thyroid; Musculoskeletal; Skin/Connective Tissue;
Reported Health Effect(s):	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
HERO ID:	62965

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

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):	Gastrointestinal
Reported Health Effect(s):	Histopathology (esophagus, stomach, duodenum, jejunum, tongue, salivary gland, ileum, colon, cecum, rectum)
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 Substance	High	The test substance is volatile and was mixed fresh daily.
	Metric 8:	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.

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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):	Gastrointestinal
Reported Health Effect(s):	Histopathology (esophagus, stomach, duodenum, jejunum, tongue, salivary gland, ileum, colon, cecum, rectum)
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: Confounding / Variable Control				
	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	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 forestomach was not shown) were not shown for each study group, but results were described in the text.

Overall Quality Determination Uninformative

Study Citation:	Dow Chemical, (2014). [Redacted] Investigation of the mode of action for 1,2-dichloroethane-induced mammary tumors in female F344/DuCrl rats.
Health Outcome(s):	Genotoxicity (Genotoxicity)
Reported Health Effect(s):	Comet assay on mammary gland cells
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 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 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				
	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 using a computer program designed to increase the probability of uniform group mean weights.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	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	Test substance was administered consistently across study groups.
	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				
	Metric 13:	Test Animal Characteristics	High	The species, strain, source, starting body weight, and age were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were fully reported and consistent between the groups.
	Metric 15:	Number of Animals per Group	Medium	The number of animals/group was appropriate (n=28).
Domain 5: Outcome Assessment				

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Study Citation:	Dow Chemical, (2014). [Redacted] Investigation of the mode of action for 1,2-dichloroethane-induced mammary tumors in female F344/DuCrl rats.
Health Outcome(s):	Genotoxicity (Genotoxicity)
Reported Health Effect(s):	Comet assay on mammary gland cells
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
	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: Confounding / Variable Control				
	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:	Dow Chemical, (2014). [Redacted] Investigation of the mode of action for 1,2-dichloroethane-induced mammary tumors in female F344/DuCrl rats.
Health Outcome(s):	Nutritional/Metabolic; Mortality; Reproductive/Developmental; Clinical signs (Clinical Signs);
Reported Health Effect(s):	Nutritional/Metabolic: Body weight and food intake; Mortality: Mortality and morbididty; Reproductive/Developmental: Serum prolactin levels, morphometry 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'-Ethylenebis glutathione (EBG), DNA adducts 8-Hydroxy-2'-deoxyguanosine (8-OH dG), S-(2- guanylethyl) glutathione (GEG), and DNA damage (Comet assay) in 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:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	10609985

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	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 Characterization				
	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 Animals				
	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.

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Study Citation:	Dow Chemical, (2014). [Redacted] Investigation of the mode of action for 1,2-dichloroethane-induced mammary tumors in female F344/DuCrl rats.
Health Outcome(s):	Nutritional/Metabolic; Mortality; Reproductive/Developmental; Clinical signs (Clinical Signs);
Reported Health Effect(s):	Nutritional/Metabolic: Body weight and food intake; Mortality: Mortality and morbididty; Reproductive/Developmental: Serum prolactin levels, morphometry 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'-Ethylenebis glutathione (EBG), DNA adducts 8-Hydroxy-2'-deoxyguanosine (8-OH dG), S-(2- guanylethyl) glutathione (GEG), and DNA damage (Comet assay) in 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:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	10609985

Domain	Metric		Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was appropriate (n=28).
Domain 5: Outcome Assessment				
	Metric 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.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Assessment protocol was reported and assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate and reported in results.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding of assessors was not necessary.
	Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.
Domain 6: Confounding / Variable Control				
	Metric 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.
	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. All animals were accounted for in results, and there was no indication of disease.
	Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis of data was reported and appropriate.
	Metric 24:	Reporting of Data	High	All Outcomes: Data were fully reported for outcomes of interest. Individual animal results are reported.

Overall Quality Determination **High**

Study Citation:	Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
Duration:	Short-term (>1-30 days) Inhalation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	625286

Domain	Metric		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 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				
	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				
	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. 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				
	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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome methodology (Body weight) was assessed appropriately.

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Study Citation:	Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
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 Control				
	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). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
Duration:	Short-term (>1-30 days) Gavage
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	625286

Domain	Metric		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 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				
	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				
	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 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	The route (gavage) was appropriate for test substance.
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 Assessment				
	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.

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Study Citation:	Dow Chemical, (2006). 1,2-Dichloroethane (EDC): Limited pharmacokinetics and metabolism study in Fischer 344 rats.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
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: Confounding / Variable Control				
	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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
Duration:	Short-term (>1-30 days) Short-term; 2-weeks
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 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 Characterization				
	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				
	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.

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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):	Mortality
Reported Health Effect(s):	Mortality
Duration:	Short-term (>1-30 days) Short-term; 2-weeks
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 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 Assessment				
	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: Confounding / Variable Control				
	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 causes when known.

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights, growth, food intake
Duration:	Short-term (>1-30 days) Short-term; 2-weeks
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 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 Characterization				
	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				
	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.

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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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights, growth, food intake
Duration:	Short-term (>1-30 days) Short-term; 2-weeks
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 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 Assessment				
	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:	Consistency of Outcome Assessment	High	Based on the information provided, animals from all groups were consistently assessed.
	Metric 18:	Sampling Adequacy	High	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: Confounding / Variable Control				
	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 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 Outcome(s):	Renal/Kidney; Endocrine (Endocrine); Reproductive/Developmental; Hepatic/Liver;
Reported Health Effect(s):	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.;
Duration:	Short-term (>1-30 days) Short-term; 2-weeks
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	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:	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.
Domain 3: Exposure Characterization				
	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				

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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):	Renal/Kidney; Endocrine (Endocrine); Reproductive/Developmental; Hepatic/Liver;
Reported Health Effect(s):	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.;
Duration:	Short-term (>1-30 days) Short-term; 2-weeks
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	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 Assessment				
	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.

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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):	Renal/Kidney; Endocrine (Endocrine); Reproductive/Developmental; Hepatic/Liver;
Reported Health Effect(s):	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.;
Duration:	Short-term (>1-30 days) Short-term; 2-weeks
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1772372

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: Confounding / Variable Control				
	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 Quality Determination High

Study Citation:	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 Outcome(s):	Immune/Hematological; Renal/Kidney; Reproductive/Developmental; Nutritional/Metabolic; Lung/Respiratory; Hepatic/Liver; Mortality;
Reported Health Effect(s):	Immune/Hematological: Relative spleen weight, spleen necropsy and histopathology; Renal/Kidney: Kidney weights were recorded and kidneys were examined at histology.; Reproductive/Developmental: Relative testicular weight; testes necropsy/histopathology with incidence of lesions; Nutritional/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;
Duration:	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 Substance				
	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				
	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 Characterization				
	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				

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Study Citation:	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 Outcome(s):	Immune/Hematological; Renal/Kidney; Reproductive/Developmental; Nutritional/Metabolic; Lung/Respiratory; Hepatic/Liver; Mortality;
Reported Health Effect(s):	Immune/Hematological: Relative spleen weight, spleen necropsy and histopathology; Renal/Kidney: Kidney weights were recorded and kidneys were examined at histology.; Reproductive/Developmental: Relative testicular weight; testes necropsy/histopathology with incidence of lesions; Nutritional/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;
Duration:	Short-term (>1-30 days) 30 days (inhalation)
Chemical:	1,1-Dichloroethane- 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 Husbandry Conditions	High	All Outcomes: Husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: There were 10-12 animals per exposure group.
Domain 5: Outcome 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	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.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Respiratory rate was not measured.
	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 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 Quality Determination High

Study Citation:	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 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:	Short-term (>1-30 days) 30 days (intraperitoneal)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200386

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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 Characterization				
	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.

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Study Citation:	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 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:	Short-term (>1-30 days) 30 days (intraperitoneal)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200386

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 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 deficiency 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: Confounding / Variable Control				
	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.
	Metric 24:	Reporting of Data	Low	All Outcomes: Data for exposure-related findings were not shown for each study group, but results were described in the text.

Overall Quality Determination — Medium

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.
Health Outcome(s):	Hepatic/Liver
Reported Health 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 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				
	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				
	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 Characterization				
	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				

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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.
Health Outcome(s): Hepatic/Liver
Reported Health 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 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
	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.
Domain 5: Outcome Assessment				
	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.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Respiratory rates were not assessed or reported. This is a potentially confounding factor.
	Metric 22:	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 Quality Determination High

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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain weight (wet and dry), blood brain barrier permeability.
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	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				
	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				
	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 Administration	High	Test substance was administered consistently across study groups.
	Metric 9:	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 Dose/Concentration Spacing	Medium	Only one exposure group was studied, a NOAEL was not obtained.
	Metric 12:	Exposure Route and Method	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 Husbandry Conditions	Medium	Light-dark cycle was not reported.
	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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain weight (wet and dry), blood brain barrier permeability.
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
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable 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	High	Data were adequately reported.

Overall Quality Determination Uninformative

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 Outcome(s):	Mortality; Clinical signs (Clinical signs);
Reported Health Effect(s):	Mortality: Mortality; Clinical signs (Clinical signs): Poisoning symptoms (tremors, forelimb flexure).;
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).
	Metric 5:	Positive Controls	N/A	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 Substance	Low	All Outcomes: Storage of test substance were not adequately reported given the volatility of the test substance.
	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: 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	All Outcomes: Exposure was for 3.5 hours a day, up to 3 days.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Only one exposure group was studied, a NOAEL was not obtained.
	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 Husbandry Conditions	Medium	All Outcomes: Light-dark cycle was not reported.
	Metric 15:	Number of Animals per Group	Medium	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 of interest.
	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.

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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 Outcome(s):	Mortality; Clinical signs (Clinical signs);
Reported Health Effect(s):	Mortality: Mortality; Clinical signs (Clinical signs): Poisoning symptoms (tremors, forelimb flexure).;
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 / Variable Control			
	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 Uninformative

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
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	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				
	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				
	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 Administration	High	Test substance was administered consistently across study groups.
	Metric 9:	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 Dose/Concentration Spacing	Medium	Only one exposure group was studied, a NOAEL was not obtained.
	Metric 12:	Exposure Route and Method	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 Husbandry Conditions	Medium	Light-dark cycle was not reported.
	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight
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 / Variable 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 Uninformative

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 Outcome(s):	Neurological/Behavioral; Nutritional/Metabolic; Mortality;
Reported Health Effect(s):	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;
Duration:	Short-term (>1-30 days) 3 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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.
	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 Administration	High	All Outcomes: Exposure was administered consistently across study groups.
	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.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Only one concentration was studied; concentration was justified based on effects in previous publications.
	Metric 12:	Exposure Route and Method	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 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 (n=6).
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodology were appropriate.
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: Details of outcome assessment protocol were limited.

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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 Outcome(s):	Neurological/Behavioral; Nutritional/Metabolic; Mortality;
Reported Health Effect(s):	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;
Duration:	Short-term (>1-30 days) 3 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	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: Confounding / Variable Control				
	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 Uninformative

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.
Health Outcome(s):	Renal/Kidney; Nutritional/Metabolic;
Reported Health Effect(s):	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); Nutritional/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 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 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 Design				
	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 Administration	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	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 Animals				
	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				

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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.
Health Outcome(s):	Renal/Kidney; Nutritional/Metabolic;
Reported Health Effect(s):	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); Nutritional/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
	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: Confounding / Variable Control				
	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 Uninformative

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 Outcome(s):	Mortality
Reported Health Effect(s):	Lethality
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 Substance				
	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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not provided.
	Metric 8:	Consistency of Exposure Administration	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.
Domain 4: Test Animals				
	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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Lethality
Duration:	Short-term (>1-30 days) Short-term
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4309

Domain	Metric		Rating	Comments
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome (lethality).
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Uninformative	Only one animal/dose was studied.
	Metric 19:	Blinding of Assessors	N/A	Lethality was evaluated.
	Metric 20:	Negative Control Response	High	The negative control response was adequate for lethality.
Domain 6: Confounding / Variable Control				
	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 differences 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 Uninformative

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 Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Histopathology of lung tissue
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 Substance				
	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).
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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not provided.
	Metric 8:	Consistency of Exposure Administration	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.
Domain 4: Test Animals				
	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				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome (lethality).
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.

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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 Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Histopathology of lung tissue
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: Confounding / Variable Control				
	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 differences 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 Uninformative

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 Outcome(s):	Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Neurological/Behavioral; Immune/Hematological; Lung/Respiratory;
Reported Health Effect(s):	Nutritional/Metabolic: body weight, gross necropsy; Hepatic/Liver: liver weight, gross necropsy; Renal/Kidney: kidney weight, gross necropsy; Neurological/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:	Short-term (>1-30 days) 14 day
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
	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	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
Domain 4: Test Animals				

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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 Outcome(s):	Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Neurological/Behavioral; Immune/Hematological; Lung/Respiratory;
Reported Health Effect(s):	Nutritional/Metabolic: body weight, gross necropsy; Hepatic/Liver: liver weight, gross necropsy; Renal/Kidney: kidney weight, gross necropsy; Neurological/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:	Short-term (>1-30 days) 14 day
Chemical:	1,1-Dichloroethane- 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 Assessment				
	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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: there were no reported differences among 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
	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 Quality Determination 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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Relative liver weight, serum ALT, AST, total cholesterol and triglycerides, histopathology and apoptosis (immunohistochemistry)
Duration:	Short-term (>1-30 days) 5 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4697150

Domain	Metric		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	Low	The source of the test substance was Sigma-Aldrich (St. Louis, Missouri). The batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	The purity of test substance was reported to be >99.8%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Low	It is not clear if the negative control group were untreated or sham treated.
	Metric 5:	Positive Controls	N/A	A positive control was not needed.
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly divided into groups.
Domain 3: Exposure Characterization				
	Metric 7:	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.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration were limited in this study and in cited reference.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Measured concentrations in chamber were not reported.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency was appropriate (6 hours/day).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups were sufficient to obtain a range of responses.
	Metric 12:	Exposure Route and Method	Uninformative	The type of inhalation chamber used is not reported. Cited reference also does not report the type of chamber.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were adequately reported.
	Metric 15:	Number of Animals per Group	Low	The numbers of animals/group exposure were not reported.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Outcome methodology was appropriate for intended outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	Medium	Details regarding the outcome assessment protocols were limited; however, this is unlikely to impact results.

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Relative liver weight, serum ALT, AST, total cholesterol and triglycerides, histopathology and apoptosis (immunohistochemistry)
Duration:	Short-term (>1-30 days) 5 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4697150

Domain	Metric		Rating	Comments
	Metric 18:	Sampling Adequacy	Medium	It is unclear how many animals were evaluated in each group. Study states "Data are presented as means ± 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.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not needed for the outcomes assessed.
	Metric 20:	Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant and therefore respiratory rate should be reported.
	Metric 22:	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 analysis was performed and appropriate.
	Metric 24:	Reporting of Data	Medium	Representative photos of histology and apoptosis are shown without any quantitative analysis to severity.

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 Pharmacology 7(1):37-44.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary glucose and protein; renal histopathology
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 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	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 Characterization				
	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 Dose/Concentration Spacing	Medium	The one dose studied was the highest one that did not cause lethality.
	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 mice 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	The number of animals/group were not reported.
Domain 5: Outcome Assessment				
	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.

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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 Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary glucose and protein; renal histopathology
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 / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Potential confounding variables 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	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:	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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge
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 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
	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	preparation of the test substance was reported and appropriate. storage was not reported
	Metric 8:	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 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 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 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.

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge
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
	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: Confounding / Variable Control				
	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

Overall Quality Determination — High

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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge
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
	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	preparation of the test substance was reported and appropriate. storage was not reported
	Metric 8:	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 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 substance.
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 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 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	Medium	outcome assessment were previously cited and briefly described and appeared to be carried out consistently across groups

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	lymphocyte stimulation, alveolar macrophage assay, pulmonary bactericidal activity, streptococcus aerosol challenge
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
	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: Confounding / Variable Control				
	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

Overall Quality Determination — 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 Outcome(s):	Mortality; Hepatic/Liver; Renal/Kidney; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Death; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Renal/Kidney: Gross 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
Domain 1: Test Substance				
	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: 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, 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	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. 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 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.

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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 Outcome(s):	Mortality; Hepatic/Liver; Renal/Kidney; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Death; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Renal/Kidney: Gross 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
Domain 4: Test Animals				
	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 Assessment				
	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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	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.

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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 Outcome(s):	Mortality; Hepatic/Liver; Renal/Kidney; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Death; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol; Renal/Kidney: Gross 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		**Uninformative**	

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 Outcome(s):	Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic;
Reported Health Effect(s):	Renal/Kidney: Gross examinations; histology; organ weights; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and 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:	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: 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, 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	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. 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 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 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	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.
Domain 4: Test Animals				

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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 Outcome(s):	Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic;
Reported Health Effect(s):	Renal/Kidney: Gross examinations; histology; organ weights; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and 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
	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: Outcome Assessment				
	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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	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	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 comparison.; 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.

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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 Outcome(s):	Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic;
Reported Health Effect(s):	Renal/Kidney: Gross examinations; histology; organ weights; Hepatic/Liver: Gross examinations; histology; organ weights; liver lipid analysis; free and 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		**Uninformative**	

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 Outcome(s):	Mortality
Reported Health Effect(s):	Death
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:	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 Design				
	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 Animals				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Death
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
	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 Assessment				
	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: Confounding / Variable Control				
	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.
	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 Uninformative

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 Outcome(s):	Nutritional/Metabolic; Mortality;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights in Part 1 (3 doses); Mortality: Only in Part 1 (3 doses);
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 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 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				
	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 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 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				
	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 Assessment				
	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.

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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 Outcome(s):	Nutritional/Metabolic; Mortality;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights in Part 1 (3 doses); Mortality: Only in Part 1 (3 doses);
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 Control				
	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 Uninformative

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver damage after subacute exposure to 1,2- DCE
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 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 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 Design				
	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				
	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 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 (10 days).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Concentrations were adequate to obtain a range of responses.
	Metric 12:	Exposure Route and Method	Uninformative	A static inhalation chamber was used.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Age was not 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 /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.

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver damage after subacute exposure to 1,2- DCE
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 21: Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant therefore respiratory rate should be 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	High	Statistical analysis was performed and appropriate.
	Metric 24: Reporting of Data	High	All outcome data were reported adequately.

Overall Quality Determination Uninformative

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver damage after subacute exposure to 1,2- DCE
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 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 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 Design				
	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				
	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 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 (10 days).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only one concentration was studied; concentration was justified based on effects in previous findings.
	Metric 12:	Exposure Route and Method	Uninformative	A static inhalation chamber was used.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Age was not 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 /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.

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver damage after subacute exposure to 1,2- DCE
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 21: Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant therefore respiratory rate should be 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	High	Statistical analysis was performed and appropriate.
	Metric 24: Reporting of Data	High	All outcome data were reported adequately.

Overall Quality Determination Uninformative

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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Open field test and mechanistic endpoints
Duration:	Short-term (>1-30 days) Short-term 10 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1522109

Domain	Metric		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	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 Design				
	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				
	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 Administration	High	Exposure was administered consistently across study groups.
	Metric 9:	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 Animals				
	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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Open field test and mechanistic endpoints
Duration:	Short-term (>1-30 days) Short-term 10 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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 / Variable Control				
	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 Uninformative

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 Outcome(s):	Mortality; Neurological/Behavioral;
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 mortalityrates 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:	Short-term (>1-30 days) Part 1: 3 days- 3 different concentrations
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4453007

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/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				
	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 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 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.
	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				
	Metric 13:	Test Animal Characteristics	Medium	Mortality: Age was not reported.; Neurological/Behavioral: 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 (n=6).
Domain 5: Outcome Assessment				

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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 Outcome(s):	Mortality; Neurological/Behavioral;
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 mortalityrates 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:	Short-term (>1-30 days) Part 1: 3 days- 3 different concentrations
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4453007

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: Confounding / Variable Control				
	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	Mortality: Mortality data are reported for all groups but data on poisoned symptoms are not adequately reported.; Neurological/Behavioral: Representative photos were shown for histology and observations were reported. No quantitative data was reported.

Overall Quality Determination Uninformative

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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	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:	Short-term (>1-30 days) Part 2: 1.2 g/m3; 2-3 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4453007

Domain	Metric		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	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				
	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 Characterization				
	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 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 Dose/Concentration Spacing	Medium	Only one concentration was studied; concentration was justified based on effects in previous findings.
	Metric 12:	Exposure Route and Method	Uninformative	A static inhalation chamber was used.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Age was not 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 /group were appropriate for the study type (n=6).
Domain 5: Outcome Assessment				
	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.
Domain 6: Confounding / Variable Control				

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	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:	Short-term (>1-30 days) Part 2: 1.2 g/m3; 2-3 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4453007

Domain	Metric		Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant therefore respiratory rate should be 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	High	Statistical analysis was performed and appropriate.
	Metric 24:	Reporting of Data	High	Data was adequately reported.

Overall Quality Determination Uninformative

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 Outcome(s):	Mortality
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 mortalityrates 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-term (>1-30 days) Part 2: 1.2 g/m3; 2-3 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4453007

Domain	Metric		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	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				
	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 Characterization				
	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 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 Dose/Concentration Spacing	Medium	Only one concentration was studied; concentration was justified based on effects in previous findings.
	Metric 12:	Exposure Route and Method	Uninformative	A static inhalation chamber was used.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Age of the animals was not 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 /group were appropriate for the study type (n=6).
Domain 5: Outcome Assessment				
	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.

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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 Outcome(s):	Mortality
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 mortalityrates 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-term (>1-30 days) Part 2: 1.2 g/m3; 2-3 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4453007

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant therefore respiratory rate should be 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	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 Uninformative

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight, food consumption
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 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 ±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 ± 0.11, 363.58 ± 24.76 and 731.10 ± 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	High	2 exposure groups plus control; both NOAEL and LOAEL identified for body weight.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight, food consumption
Duration:	Short-term (>1-30 days) 28 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5555689

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 Animals				
	Metric 13:	Test Animal Characteristics	High	"According to preliminary experimental results, male mice were more sensitive to exposure of 1,2-DCE...thirty 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 tofood 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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Body weight was measured weekly.
	Metric 17:	Consistency of Outcome Assessment	High	Body weight was measured weekly.
	Metric 18:	Sampling Adequacy	High	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: Confounding / Variable Control				
	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 ± 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

Overall Quality Determination High

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver weight; serum ALT, AST, glucose, triglycerides, and free fatty acids; liver glycogen, triglycerides, and free fatty acids.
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 ±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 ± 0.11, 363.58 ± 24.76 and 731.10 ± 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:	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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Liver weight; serum ALT, AST, glucose, triglycerides, and free fatty acids; liver glycogen, triglycerides, and free fatty acids.
Duration:	Short-term (>1-30 days) 28 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5555689

Domain	Metric		Rating	Comments
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	"According to preliminary experimental results, male mice were more sensitive to exposure of 1,2-DCE...thirty 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 tofood 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 Assessment				
	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: Confounding / Variable Control				
	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 ± 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 Quality Determination — High

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):	Neurological/Behavioral
Reported Health Effect(s):	Behavioral changes, brain weight and histopathology, oxidative stress endpoints (NPSH, MDA, SOD) in the brain, and mechanistic endpoints (mRNA and 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
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.
	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.” Authors did not describe randomization process.
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	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 Dose/Concentration Spacing	Low	Single exposure level was not high enough to elicit effect on brain apical endpoints but was high enough to induce mechanistic changes.
	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 Animals				
	Metric 13:	Test Animal Characteristics	Medium	Age was not reported. ”Female Kunming mice, weighing 22 ± 2 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%.”

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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):	Neurological/Behavioral
Reported Health Effect(s):	Behavioral changes, brain weight and histopathology, oxidative stress endpoints (NPSH, MDA, SOD) in the brain, and mechanistic endpoints (mRNA and 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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	respiratory rate 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 that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	”Significant differences were evaluated by a one-way analysis ofvariance (ANOVA) followed by the post hoc Student-Newman-Keulstest. Joint effects were evaluated by ANOVA of with a factorialdesign. 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 — Uninformative

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):	Mortality
Reported Health Effect(s):	Mortality
Duration:	Short-term (>1-30 days) 3 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5556105

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	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.
	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 Animals				
	Metric 13:	Test Animal Characteristics	Medium	Age was not reported. ”Female Kunming mice, weighing 22 ± 2 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

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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):	Mortality
Reported Health Effect(s):	Mortality
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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Mortality was assessed during study
	Metric 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.
	Metric 18:	Sampling Adequacy	High	All animals evaluated for mortality
	Metric 19:	Blinding of Assessors	N/A	Not relevant for mortality
	Metric 20:	Negative Control Response	High	There were no control deaths.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	respiratory rate 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 that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed for mortality but incidences were reported, enabling independent analysis
	Metric 24:	Reporting of Data	High	Mortality rates reported by exposure group.

Overall Quality Determination Uninformative

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 Outcome(s):	Reproductive/Developmental; Nutritional/Metabolic;
Reported Health Effect(s):	Reproductive/Developmental: Testis and epididymis weight, sperm count, sperm motility, morphological analysis of spermatozoa, histology on testis and 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) 4 week
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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.
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 Administration	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	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 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.

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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 Outcome(s):	Reproductive/Developmental; Nutritional/Metabolic;
Reported Health Effect(s):	Reproductive/Developmental: Testis and epididymis weight, sperm count, sperm motility, morphological analysis of spermatozoa, histology on testis and 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) 4 week
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4453049

Domain	Metric		Rating	Comments
Domain 5: Outcome Assessment				
	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	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: Confounding / Variable Control				
	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

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 Outcome(s):	Reproductive/Developmental; Nutritional/Metabolic;
Reported Health Effect(s):	Reproductive/Developmental: Testis and epididymis weight, sperm count, sperm motility, morphological analysis of spermatozoa, histology on testis and 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
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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	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	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 Administration	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	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.
	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 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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodology were appropriate.

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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 Outcome(s):	Reproductive/Developmental; Nutritional/Metabolic;
Reported Health Effect(s):	Reproductive/Developmental: Testis and epididymis weight, sperm count, sperm motility, morphological analysis of spermatozoa, histology on testis and 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
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: Confounding / Variable Control				
	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

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 Outcome(s):	Genotoxicity (Genotoxicity); Genotoxicity (Genotoxicity);
Reported Health Effect(s):	Genotoxicity (Genotoxicity): Comet assay on spermatozoa; Genotoxicity (Genotoxicity): Comet assay on spermatozoa;
Duration:	Short-term (>1-30 days) 1 week
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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	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 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	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 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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment and methodology were appropriate.

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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 Outcome(s):	Genotoxicity (Genotoxicity); Genotoxicity (Genotoxicity);
Reported Health Effect(s):	Genotoxicity (Genotoxicity): Comet assay on spermatozoa; Genotoxicity (Genotoxicity): Comet assay on spermatozoa;
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: Confounding / Variable Control				
	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 — Uninformative

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 Effect(s):	Nutritional/Metabolic: body weight, food consumption; Nutritional/Metabolic: body weight, food consumption;
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 Substance				
	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 Characterization				
	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.

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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 Effect(s):	Nutritional/Metabolic: body weight, food consumption; Nutritional/Metabolic: body weight, food consumption;
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
	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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Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic;
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)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	194588

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: Confounding / Variable Control				
	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

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):	Hepatic/Liver
Reported Health Effect(s):	liver fat content, serum total protein, cholesterol, ALT, AST
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 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.

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver fat content, serum total protein, cholesterol, ALT, AST
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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				
	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 Assessment				
	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				

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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 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

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):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Renal/Kidney;
Reported Health Effect(s):	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

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.

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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):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Renal/Kidney;
Reported Health Effect(s):	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

Domain	Metric		Rating	Comments
	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 Assessment				

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Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Renal/Kidney;
Reported Health Effect(s):	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

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 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 for the outcome of interest.

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Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Neurological/Behavioral; Nutritional/Metabolic; Reproductive/Developmental; Missing 'other' target organ (Adrenal glands, pancreas, parathyroid); Renal/Kidney;
Reported Health Effect(s):	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);
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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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. 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 assessed initially, which is standard practice.
	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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Reported Health Effect(s):	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

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
	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 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).

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Reported Health Effect(s):	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
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HERO ID:	62965

Domain	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.

Overall Quality Determination High

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):	Hepatic/Liver
Reported Health Effect(s):	Clinical chemistry (ALP, AST, ALT, cholesterol [10-day only]), organ weight (liver), gross necropsy (liver), histopathology (liver)
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 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 Substance	High	The test substance is volatile and was mixed fresh daily.
	Metric 8:	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 90-day study.

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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):	Hepatic/Liver
Reported Health Effect(s):	Clinical chemistry (ALP, AST, ALT, cholesterol [10-day only]), organ weight (liver), gross necropsy (liver), histopathology (liver)
Duration:	Subchronic (>30-91 days) 90 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 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: Confounding / Variable Control				
	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.

Overall Quality Determination High

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):	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	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 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):	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	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 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 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	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.
Domain 6: Confounding / Variable Control				
	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	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.

Overall Quality Determination High

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):	Gastrointestinal
Reported Health Effect(s):	Histopathology (esophagus, stomach, duodenum, jejunum, tongue, salivary gland, ileum, colon, cecum, rectum)
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 Substance	High	The test substance is volatile and was mixed fresh daily.
	Metric 8:	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.

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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):	Gastrointestinal
Reported Health Effect(s):	Histopathology (esophagus, stomach, duodenum, jejunum, tongue, salivary gland, ileum, colon, cecum, rectum)
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 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: Confounding / Variable Control				
	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

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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights, growth, food intake
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 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 Characterization				
	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				
	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.

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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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights, growth, food intake
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	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: Confounding / Variable Control				
	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 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 Outcome(s):	Mortality
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
Domain 1: Test Substance				
	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 Characterization				
	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				
	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.

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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):	Mortality
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: Confounding / Variable Control				
	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.
Health Outcome(s):	Gastrointestinal; Musculoskeletal; Lung/Respiratory;
Reported Health Effect(s):	Gastrointestinal: Histopathology (stomach, salivary glands, intestines); Musculoskeletal: Histopathology (muscle); Lung/Respiratory: Histopathology (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 Substance				
	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:	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.
Domain 3: Exposure Characterization				
	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				

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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):	Gastrointestinal; Musculoskeletal; Lung/Respiratory;
Reported Health Effect(s):	Gastrointestinal: Histopathology (stomach, salivary glands, intestines); Musculoskeletal: Histopathology (muscle); Lung/Respiratory: Histopathology (lungs);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1772372

Domain	Metric		Rating	Comments
	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 Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Gastrointestinal: 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.; 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 high-dose 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.

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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):	Gastrointestinal; Musculoskeletal; Lung/Respiratory;
Reported Health Effect(s):	Gastrointestinal: Histopathology (stomach, salivary glands, intestines); Musculoskeletal: Histopathology (muscle); Lung/Respiratory: Histopathology (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: Confounding / Variable Control				
	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 severity.

Overall Quality Determination Medium

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):	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
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	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:	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.
Domain 3: Exposure Characterization				
	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.

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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):	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
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1772372

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 Animals				
	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 Assessment				

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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):	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
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1772372

Domain	Metric		Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Medium	Renal/Kidney: 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). 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.
	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.

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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):	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
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	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 high-dose 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.
	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: Confounding / Variable Control				
	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.

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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):	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
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1772372

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 assessment. Some animals were missing from some endpoints (e.g., not all 10 animals were sampled), but the reason for this was not specified.; 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 (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 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	Low	All Outcomes: Continuous data were reported as means without measures of variance. Histopathology results included measures of severity.

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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):	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
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1772372

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 Outcome(s):	Mortality; Nutritional/Metabolic; Hepatic/Liver;
Reported Health Effect(s):	Mortality: Mortality; 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;
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	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 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).
	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				

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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 Outcome(s):	Mortality; Nutritional/Metabolic; Hepatic/Liver;
Reported Health Effect(s):	Mortality: Mortality; 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;
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
	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 Assessment				
	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 Control				
	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:	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):	Mortality; Nutritional/Metabolic; Hepatic/Liver;
Reported Health Effect(s):	Mortality: Mortality; 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;
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
	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 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 Outcome(s):	Cardiovascular
Reported Health Effect(s):	Heart histology (1,2-dichloroethane only)
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:	Test Substance Purity	High	The purity of 1,2-dichloroethane was > 99%.
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 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	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				

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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 Outcome(s):	Cardiovascular
Reported Health Effect(s):	Heart histology (1,2-dichloroethane only)
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
	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	High	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 / Variable Control				
	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	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

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):	Immune/Hematological
Reported Health Effect(s):	Blood counts - specific parameters not specified (rats, rabbits, and cats only)
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:	Test Substance Purity	High	The purity of 1,2-dichloroethane was > 99%.
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 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	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				

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Blood counts - specific parameters not specified (rats, rabbits, and cats only)
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
	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 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.
	Metric 17:	Consistency of Outcome Assessment	Low	The time points in which hematology parameters were assessed were not specified.
	Metric 18:	Sampling Adequacy	High	Blood counts 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	Hematology data for control animals were not reported.
Domain 6: Confounding / Variable Control				
	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 results across groups).
	Metric 24:	Reporting 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.”

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 Outcome(s):	Renal/Kidney
Reported Health 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").
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:	Test Substance Purity	High	The purity of 1,2-dichloroethane was > 99%.
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 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	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				

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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 Outcome(s):	Renal/Kidney
Reported Health 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").
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
	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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Renal/Kidney
Reported Health 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”).
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**	

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):	Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney;
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").;
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:	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 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).

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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 Outcome(s):	Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney;
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").;
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 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).

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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 Outcome(s):	Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney;
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").;
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 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).
Domain 5: Outcome Assessment				
	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.

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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 Outcome(s):	Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney;
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").;
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 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 / Variable Control				
	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:	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):	Immune/Hematological; Immune/Hematological; Hepatic/Liver; Renal/Kidney;
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”).;
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 23:	Data Presentation and Analysis	N/A	Immune/Hematological: Statistical analysis was not performed/not necessary (results 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 clinical-chemical 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:	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):	Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;
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: Mortality;
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:	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 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).

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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 Outcome(s):	Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;
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: Mortality;
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 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

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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 Outcome(s):	Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;
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: Mortality;
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 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 not 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

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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 Outcome(s):	Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;
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: Mortality;
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 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 results 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 was evaluated (e.g., the study stated that rats typically died after 10-17 exposures).; 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 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.; Mortality: 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.

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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 Outcome(s):	Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;
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: Mortality;
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 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 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	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.

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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 Outcome(s):	Hepatic/Liver; Renal/Kidney; Lung/Respiratory; Mortality; Mortality;
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: Mortality;
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	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: 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: 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 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 Outcome(s):	Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);
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); 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
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 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).

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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 Outcome(s):	Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);
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); 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
	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 Outcome(s):	Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);
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); 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
	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 not reported.; Cardiovascular: 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

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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 Outcome(s):	Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);
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); 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
	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 (the surviving animal). Control animals were presumably assessed histologically 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.
	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.

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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 Outcome(s):	Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);
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); 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
	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: Confounding / Variable Control				
	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 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

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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 Outcome(s):	Cardiovascular; Endocrine; Cardiovascular; Cardiovascular; Endocrine (Adrenal glands);
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); 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

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):	Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;
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:	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 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).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	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 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.

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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 Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;
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 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 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 Assessment				
	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 / Variable Control				
	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.

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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 Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;
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

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):	Nutritional/Metabolic
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
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:	Test Substance Purity	High	The purity of 1,2-dichloroethane was > 99%.
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 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				

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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 Outcome(s):	Nutritional/Metabolic
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
	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	Low	According to the methods, body weights were repeatedly monitored during the experimental period.
	Metric 17:	Consistency of Outcome Assessment	Low	The time points at which body weights were assessed were not reported.
	Metric 18:	Sampling Adequacy	High	Body weights were presumably 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 control animals was not reported.
Domain 6: Confounding / Variable Control				
	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 (a 10% change in body weight relative to controls could be used to determine biological significance).
	Metric 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

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):	Mortality
Reported Health Effect(s):	Mortality
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	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				
	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	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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Mortality
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 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).
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.
Domain 6: Confounding / Variable Control				
	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, 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 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 Outcome(s):	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").;
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 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 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).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	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 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 Outcome(s):	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").;
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 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 Assessment				
	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: Confounding / Variable Control				
	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:	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):	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").;
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.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Immune/Hematological;
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				
	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 Characterization				
	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.

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Study Citation:	IRFMN, (1987). Report on the clinical chemistry results after 18 months inhalatory exposure - ethylene dichloride.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Immune/Hematological;
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
	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.

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Study Citation:	IRFMN, (1987). Report on the clinical chemistry results after 18 months inhalatory exposure - ethylene dichloride.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Immune/Hematological;
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
	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				

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Study Citation:	IRFMN, (1987). Report on the clinical chemistry results after 18 months inhalatory exposure - ethylene dichloride.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Immune/Hematological;
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
	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

Study Citation:	Kettering Laboratory, (1943). The physiological effects upon rabbits of exposure to 1,2-dichloroethane and 1,2-dibromoethane.
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory rate, 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
Domain 1: Test Substance				
	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				
	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 Substance	Low	There was no mention of the method and equipment used to generate the test substance.
	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.
	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				
	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.

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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 Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory rate, 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
	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	High	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 20:	Negative Control Response	Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding / Variable Control				
	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 (2 rabbit/group)
	Metric 24:	Reporting of Data	High	Data for clinical signs were reported in text for each animal.

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 Outcome(s):	Gastrointestinal
Reported Health 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
Domain 1: Test Substance				
	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				
	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 Substance	Low	There was no mention of the method and equipment used to generate the test substance.
	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.
	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				
	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	Incidence of diarrhea was reported for each animal in text.

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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 Outcome(s):	Gastrointestinal
Reported Health 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
	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	High	It appears that all animals were evaluated for clinical signs.
	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 / Variable Control				
	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 (2 rabbit/group)
	Metric 24:	Reporting of Data	High	Findings were reported in text for each animal.

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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical signs
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
Domain 1: Test Substance				
	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				
	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 Substance	Low	There was no mention of the method and equipment used to generate the test substance.
	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.
	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				
	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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical signs
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. 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 20:	Negative Control Response	Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding / Variable Control				
	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 (2 rabbit/group)
	Metric 24:	Reporting of Data	High	Data for clinical signs were reported in text for each animal.

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 Outcome(s):	Mortality
Reported Health Effect(s):	Deaths
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
Domain 1: Test Substance				
	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				
	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 Substance	Low	There was no mention of the method and equipment used to generate the test substance.
	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.
	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				
	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	Death of animals was reported in text.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Deaths
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	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.
	Metric 18:	Sampling Adequacy	High	All animals were monitored for mortality
	Metric 19:	Blinding of Assessors	N/A	Blinding is not necessary for this outcome.
	Metric 20:	Negative Control Response	Uninformative	Diarrhea, decreased body weight and mortality occurred in control rabbits.
Domain 6: Confounding / Variable Control				
	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 (2 rabbit/group)
	Metric 24:	Reporting of Data	High	Mortality data was reported in text.

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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Hematology
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
Domain 1: Test Substance				
	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				
	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 Substance	Low	There was no mention of the method and equipment used to generate the test substance.
	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.
	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				
	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	Low	Methods for hematology assessment were not reported.

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Hematology
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. Details regarding the timing of hematology assessment were not reported.
	Metric 18:	Sampling Adequacy	Low	It was not clear whether if hematology analysis was performed for all exposed rabbits.
	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 / Variable Control				
	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 (2 rabbit/group)
	Metric 24:	Reporting of Data	Uninformative	The report does not provide data for specific exposure groups.

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Decreased body weight
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
Domain 1: Test Substance				
	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				
	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 Substance	Low	There was no mention of the method and equipment used to generate the test substance.
	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.
	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				
	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	Medium	Body weight gain was reported for each animal at the end of the treatment (mean body weights were not shown).

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Decreased body weight
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 / Variable Control				
	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 (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 Uninformative

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)
Duration:	Subchronic (>30-91 days) 7 Weeks (promotion protocol)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200479

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	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 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	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				
	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 was appropriate and sensitive for tumor promotion potential.
	Metric 17:	Consistency of Outcome Assessment	High	Timing of necropsy was consistent across groups.
	Metric 18:	Sampling Adequacy	High	Sample size (n = 9-10) was adequate for assessment of tumor promotion 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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Increased incidence of GGT-positive liver foci in rats dosed during promotion phase (1,1,2-TCE only)
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	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: Confounding / Variable Control				
	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 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

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Decreased body weight gain (1,1,2-TCE only)
Duration:	Subchronic (>30-91 days) 7 Weeks (promotion protocol)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200479

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 body 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 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				
	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Decreased body weight gain (1,1,2-TCE only)
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: Confounding / Variable Control				
	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

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Decreased absolute liver weight (1,1,2-TCE only)
Duration:	Subchronic (>30-91 days) 7 Weeks (promotion protocol)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200479

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 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 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				
	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.

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Decreased absolute liver weight (1,1,2-TCE only)
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: Confounding / Variable Control				
	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

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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	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
Duration:	Subchronic (>30-91 days) 90 day
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	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				
	Metric 4:	Negative and Vehicle Controls	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 Substance	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 every 3-4 days
	Metric 8:	Consistency of Exposure Administration	Medium	exposures were administered consistently across groups however water consumption was reduced in treated groups
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity as calculated from consumption.
	Metric 10:	Exposure Frequency and Duration	High	administration was appropriate for the study
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	number of groups was 3 treatment and a control and was adequate. Spacing did not encompass effects perhaps due to decreased consumption
	Metric 12:	Exposure Route and Method	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
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	animal husbandry conditions were reported and consistent
	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

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	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
Duration:	Subchronic (>30-91 days) 90 day
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 / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	decreased water consumption was reported in treated animals
	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
	Metric 23:	Data Presentation and Analysis	High	methods were described and appropriate
	Metric 24:	Reporting of Data	High	data were reported for all groups negative data were reported in text

Overall Quality Determination Uninformative

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 Outcome(s):	Lung/Respiratory; Hepatic/Liver; Nutritional/Metabolic; Neurological/Behavioral; Renal/Kidney; Mortality;
Reported Health Effect(s):	Lung/Respiratory: lung weight, gross necropsy; Hepatic/Liver: liver weight, gross necropsy; Nutritional/Metabolic: body weight, gross necropsy; Neurological/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 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
	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	Medium	All Outcomes: preparation and storage conditions were incompletely reported but reported details indicate the authors prepared the substance every 3-4 days and the amount lost was within 10%
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: exposures were administered consistently across groups however water 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
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	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
	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 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 16-24/group and was appropriate

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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 Outcome(s):	Lung/Respiratory; Hepatic/Liver; Nutritional/Metabolic; Neurological/Behavioral; Renal/Kidney; Mortality;
Reported Health Effect(s):	Lung/Respiratory: lung weight, gross necropsy; Hepatic/Liver: liver weight, gross necropsy; Nutritional/Metabolic: body weight, gross necropsy; Neurological/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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Uninformative	All Outcomes: decreased water consumption was reported in treated animals
	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
	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 Uninformative

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
Duration:	Subchronic (>30-91 days) 6-weeks-rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5441108

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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				
	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
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 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.
	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 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 / Variable Control				
	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 ± 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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
Duration:	Subchronic (>30-91 days) 6-weeks-rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5441108

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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: Confounding / Variable Control				
	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 — Uninformative

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
Duration:	Subchronic (>30-91 days) 6-weeks mice
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5441108

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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				
	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
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 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: Confounding / Variable Control				
	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 ± 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 Outcome(s):	Mortality
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
Domain 1: Test Substance				
	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 Characterization				
	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				
	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.

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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 Outcome(s):	Mortality
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 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: Confounding / Variable Control				
	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 — Uninformative

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):	Hepatic/Liver
Reported Health Effect(s):	Organ weight; histopathology; serum chemistry
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				
	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 assignedto cages by one table of random numbers and to groups byanother 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; 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 Dose/Concentration Spacing	High	6 dose-groups including controls
	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 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

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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):	Hepatic/Liver
Reported Health Effect(s):	Organ weight; histopathology; serum chemistry
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 5: Outcome Assessment				
	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: Confounding / Variable Control				
	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 Quality Determination High

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; Nutritional/Metabolic;
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
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: 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 assignedto cages by one table of random numbers and to groups byanother 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; 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				
	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 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 Outcome(s):	Mortality; Nutritional/Metabolic;
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: Confounding / Variable Control				
	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 Quality Determination High

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):	Cardiovascular; Reproductive/Developmental; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight (Testis); histopathology; Renal/Kidney: Organ weight; histopathology;
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	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 assignedto cages by one table of random numbers and to groups byanother 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; 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				
	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.

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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):	Cardiovascular; Reproductive/Developmental; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight (Testis); histopathology; Renal/Kidney: Organ weight; histopathology;
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 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 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.

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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):	Cardiovascular; Reproductive/Developmental; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight (Testis); histopathology; Renal/Kidney: Organ weight; histopathology;
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 20:	Negative Control Response	Low	Cardiovascular: Negative control-related organ weights were appropriate; histopathology data were selectively reported and did not include this target/organ system.; Reproductive/Developmental: Negative control-related organ weights were appropriate; histopathology data were selectively reported and did not include this target/organ system.; Renal/Kidney: Negative control-related organ weights and serum chemistry parameters were appropriate; histopathology data were selectively reported and did not include this target/organ system.
Domain 6: Confounding / Variable Control				
	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	Cardiovascular: Appropriate methods of statistical analyses of organ weight and histology data were used.; Reproductive/Developmental: Appropriate methods of statistical analyses of organ weight and histology data were used.; Renal/Kidney: Appropriate methods of statistical analyses of organ weights, serum chemistry, hematology, and histology data were used.
	Metric 24:	Reporting of Data	Low	Cardiovascular: 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.; Reproductive/Developmental: 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.; Renal/Kidney: Organ weight and relevant serum chemistry data were adequately presented. Histopathology results for this tissue/organ system were reported to be negative in the text, but incidence data were not provided.

Overall Quality Determination High

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 Effect(s):	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);
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	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 assignedto cages by one table of random numbers and to groups byanother 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; 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				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, age, source and initial BW were reported and were appropriate.

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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 Effect(s):	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);
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 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
Domain 5: Outcome Assessment				
	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.

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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 Effect(s):	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);
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 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:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	Low	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 Control				
	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	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.

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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 Effect(s):	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);
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 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 Uninformative

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):	Immune/Hematological
Reported Health Effect(s):	Histopathology; hematology
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				
	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 assignedto cages by one table of random numbers and to groups byanother 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; 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 Dose/Concentration Spacing	High	6 dose-groups including controls
	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 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 Assessment				
	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.

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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):	Immune/Hematological
Reported Health Effect(s):	Histopathology; hematology
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	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: Confounding / Variable Control				
	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.

Overall Quality Determination — High

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):	Gastrointestinal
Reported Health Effect(s):	Histopathology
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				
	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 assignedto cages by one table of random numbers and to groups byanother 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; 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 Dose/Concentration Spacing	High	6 dose-groups including controls
	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 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: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Methodology for 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 Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Histopathology
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 / Variable Control				
	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

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):	Neurological/Behavioral
Reported Health Effect(s):	Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea
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				
	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 assignedto cages by one table of random numbers and to groups byanother 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; 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 Dose/Concentration Spacing	High	6 dose-groups including controls
	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 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: Outcome Assessment				
	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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea
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	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: Confounding / Variable Control				
	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.

Overall Quality Determination — High

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 weight, histopathology
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				
	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 assignedto cages by one table of random numbers and to groups byanother 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; 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 Dose/Concentration Spacing	High	6 dose-groups including controls
	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	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: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	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 Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Organ weight, histopathology
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	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: Confounding / Variable Control				
	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

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):	Thyroid
Reported Health Effect(s):	Related histology
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups
	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 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 Outcome(s):	Thyroid
Reported Health Effect(s):	Related histology
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	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 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.
Domain 6: Confounding / Variable Control				
	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 Uninformative

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 Effect(s):	Survival
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 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				
	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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Animals were observed for mortality

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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 Effect(s):	Survival
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 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: Confounding / Variable 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	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

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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight, weight gain, water consumption
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups
	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 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				

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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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight, weight gain, water consumption
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	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: Confounding / Variable 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 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 ± 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.

Overall Quality Determination — High

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 Effect(s):	Survival
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups.
	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 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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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: Confounding / Variable Control				
	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 Uninformative

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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight, weight gain, water consumption
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups
	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 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				

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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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight, weight gain, water consumption
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	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 reporting.
Domain 6: Confounding / Variable Control				
	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 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 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 ± 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 — Uninformative

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; Cardiovascular; Reproductive/Developmental;
Reported Health Effect(s):	Lung/Respiratory: Organ weight, histopathology; Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight (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 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:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assignedto cages by one table of random numbers and to groups byanother 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	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 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/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 Outcome(s):	Lung/Respiratory; Cardiovascular; Reproductive/Developmental;
Reported Health Effect(s):	Lung/Respiratory: Organ weight, histopathology; Cardiovascular: Organ weight (heart), histopathology; Reproductive/Developmental: Organ weight (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: Confounding / Variable Control				
	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

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):	Ocular/Sensory; Musculoskeletal (Endocrine organs); Endocrine (Endocrine organs); Skin/Connective Tissue (Endocrine organs); Gastrointestinal;
Reported Health Effect(s):	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; Gastrointestinal: 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 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:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assignedto cages by one table of random numbers and to groups byanother 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	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				

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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):	Ocular/Sensory; Musculoskeletal (Endocrine organs); Endocrine (Endocrine organs); Skin/Connective Tissue (Endocrine organs); Gastrointestinal;
Reported Health Effect(s):	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; Gastrointestinal: 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
	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
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	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.; Gastrointestinal: 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 results 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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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):	Ocular/Sensory; Musculoskeletal (Endocrine organs); Endocrine (Endocrine organs); Skin/Connective Tissue (Endocrine organs); Gastrointestinal;
Reported Health Effect(s):	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; Gastrointestinal: 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
	Metric 20:	Negative Control Response	Low	All Outcomes: The biological responses of the negative control group(s) were not reported.
Domain 6: Confounding / Variable Control				
	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 Uninformative

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):	Neurological/Behavioral
Reported Health Effect(s):	Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups
	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 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				

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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):	Neurological/Behavioral
Reported Health Effect(s):	Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea
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: Confounding / Variable 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	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

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):	Reproductive/Developmental; Lung/Respiratory;
Reported Health Effect(s):	Reproductive/Developmental: Organ weight (Testis); histopathology; Lung/Respiratory: Organ weight, histopathology;
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:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assignedto cages by one table of random numbers and to groups byanother 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	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 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 for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.

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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):	Reproductive/Developmental; Lung/Respiratory;
Reported Health Effect(s):	Reproductive/Developmental: Organ weight (Testis); histopathology; Lung/Respiratory: Organ weight, histopathology;
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	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 Control				
	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 Uninformative

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):	Gastrointestinal; Musculoskeletal; Ocular/Sensory;
Reported Health Effect(s):	Gastrointestinal: Histopathology; Musculoskeletal: Related histology; Ocular/Sensory: Histopathology (if grossly abnormal);
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:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assignedto cages by one table of random numbers and to groups byanother 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	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 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 for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.

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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):	Gastrointestinal; Musculoskeletal; Ocular/Sensory;
Reported Health Effect(s):	Gastrointestinal: Histopathology; Musculoskeletal: Related histology; Ocular/Sensory: Histopathology (if grossly abnormal);
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	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: Confounding / Variable Control				
	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 Uninformative

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):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: Organ weight; histopathology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;
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:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assignedto cages by one table of random numbers and to groups byanother 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	High	Renal/Kidney: 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 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 for the main group, plus an additional 10 males/sex for hematology and clinical chemistry.

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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):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: Organ weight; histopathology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;
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	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: Confounding / Variable Control				
	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.

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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):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: Organ weight; histopathology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;
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 Uninformative

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):	Immune/Hematological
Reported Health Effect(s):	Histopathology; hematology
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups
	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 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				

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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):	Immune/Hematological
Reported Health Effect(s):	Histopathology; hematology
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 Control				
	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 **Uninformative**

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):	Neurological/Behavioral
Reported Health Effect(s):	Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups
	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 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				

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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):	Neurological/Behavioral
Reported Health Effect(s):	Histopathology; organ weight (brain), clinical signs included tremors, salivation, emaciation, abnormal postures, ruffled fur, and dyspnea
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	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: Confounding / Variable Control				
	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	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	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 — Uninformative

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):	Renal/Kidney
Reported Health Effect(s):	Organ weight; 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 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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups
	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 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				

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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):	Renal/Kidney
Reported Health Effect(s):	Organ weight; 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
	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 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-dichloroethane (ethylene bichloride) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies).
Health Outcome(s):	Immune/Hematological; Hepatic/Liver;
Reported Health Effect(s):	Immune/Hematological: Histopathology; hematology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;
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	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 assignedto cages by one table of random numbers and to groups byanother 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	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 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	Immune/Hematological: 10/sex/group; Hepatic/Liver: 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 Outcome(s):	Immune/Hematological; Hepatic/Liver;
Reported Health Effect(s):	Immune/Hematological: Histopathology; hematology; Hepatic/Liver: Organ weight; histopathology; serum chemistry;
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	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: Confounding / Variable Control				
	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

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):	Thyroid
Reported Health Effect(s):	Related histology
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	High	Test substance was administered consistently across study groups
	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 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				

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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):	Thyroid
Reported Health Effect(s):	Related histology
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 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.
Domain 6: Confounding / Variable 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 and histopathology
	Metric 24:	Reporting of Data	Uninformative	Histopathology results for this organ/system were not reported

Overall Quality Determination — Uninformative

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):	Skin/Connective Tissue; Endocrine;
Reported Health Effect(s):	Skin/Connective Tissue: Histology of skin; Endocrine: Histology of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.;
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:	Randomized Allocation of Animals	Medium	All Outcomes: Animals distributed to weight classes and then assignedto cages by one table of random numbers and to groups byanother 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 of 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 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	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.

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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):	Skin/Connective Tissue; Endocrine;
Reported Health Effect(s):	Skin/Connective Tissue: Histology of skin; Endocrine: Histology of related tissues/organs (Adrenal glands, pituitary gland). Could also include pancreas.;
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: Confounding / Variable Control			
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	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	All Outcomes: Histopathology results for this organ/system were not reported

Overall Quality Determination Uninformative

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):	Cardiovascular
Reported Health Effect(s):	Organ weight (heart), histopathology
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
	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 assignedto cages by one table of random numbers and to groups byanother 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 Administration	Medium	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				
	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				

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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):	Cardiovascular
Reported Health Effect(s):	Organ weight (heart), histopathology
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	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 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: Confounding / Variable Control				
	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 were adequately reported. Histopathology results for this outcome were not reported.

Overall Quality Determination Uninformative

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):	Mortality
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
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 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 (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.

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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):	Mortality
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 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 necessary for this study type.
Domain 5: Outcome Assessment				
	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				

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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):	Mortality
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 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 Uninformative

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):	Hepatic/Liver
Reported Health Effect(s):	liver fat content, serum total protein, cholesterol, ALT, AST
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 Characterization				
	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%.
	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.

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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):	Hepatic/Liver
Reported Health Effect(s):	liver fat content, serum total protein, cholesterol, ALT, AST
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				

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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):	Hepatic/Liver
Reported Health Effect(s):	liver fat content, serum total protein, cholesterol, ALT, AST
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 — Uninformative

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):	Renal/Kidney
Reported Health Effect(s):	serum urea, uric acid, glucose
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 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 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.

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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):	Renal/Kidney
Reported Health Effect(s):	serum urea, uric acid, glucose
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 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	Medium	Negative control animals responded appropriately.
Domain 6: Confounding / Variable Control				

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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):	Renal/Kidney
Reported Health Effect(s):	serum urea, uric acid, glucose
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 — Uninformative

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):	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;
Reported Health Effect(s):	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 (1,2-dichloroethane) 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 (1,2-dichloroethane).; 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).

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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):	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;
Reported Health Effect(s):	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
	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 analytically verified by the laboratory.

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Health Outcome(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;
Reported Health Effect(s):	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
	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%.; Gastrointestinal: 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%.; Mortality: 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%.
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 Characterization				

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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):	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;
Reported Health Effect(s):	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
	Metric 7:	Preparation and Storage of Test Substance	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 within 2% of nominal concentrations, indicating minimal loss or decomposition of the test substance during volatilization.; Mortality: 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 concentra-

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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):	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;
Reported Health Effect(s):	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
	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: 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 Animals				
	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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Cancer/Carcinogenesis: The outcome assessment methodology was appropriate.; Nutritional/Metabolic: The outcome assessment methodology appropriate.; Thyroid: The outcome assessment methodology appropriate.; Neurological/Behavioral: The outcome assessment methodology appropriate.; Cardiovascular: The outcome assessment methodology appropriate.; Gastrointestinal: The outcome assessment methodology appropriate.; Immune/Hematological: The outcome assessment methodology appropriate.; Hepatic/Liver: The outcome assessment methodology appropriate.; Musculoskeletal: The outcome assessment methodology appropriate.; Mortality: The outcome assessment methodology appropriate.; Renal/Kidney: The outcome assessment methodology appropriate.; Renal/Kidney: The outcome assessment methodology appropriate.; Ocular/Sensory: The outcome assessment methodology appropriate.; Lung/Respiratory: The outcome assessment methodology appropriate.; Skin/Connective Tissue: The outcome assessment methodology appropriate.

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Health Outcome(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;
Reported Health Effect(s):	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
	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.; Cardiovascular: 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.; Ocular/Sensory: 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: Confounding / Variable 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	High	All Outcomes: Exposure related findings were reported adequately.

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 Outcome(s):	Endocrine
Reported Health Effect(s):	Examine: adrenal glands, pancreas, parathyroid, pituitaryHistology: adrenal glands, parathyroid, pituitary, pancreas
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	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 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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	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.
	Metric 8:	Consistency of Exposure Administration	High	Test substance was delivered consistently across study groups.
	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 (7hr/day, 5 day/week for 2 years)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	Only one concentration was studied, this was based off the current US occupational standard.
	Metric 12:	Exposure Route and Method	Medium	Dynamic whole body was used with 12 air changes/hr.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Animal characteristics were adequately described.
	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 acceptable (50/sex/group).
Domain 5: Outcome Assessment				
	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.

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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):	Endocrine
Reported Health Effect(s):	Examine: adrenal glands, pancreas, parathyroid, pituitaryHistology: adrenal glands, parathyroid, pituitary, pancreas
Duration:	Chronic (>91 days) 2 year
Chemical:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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	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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Examine: accessory sex organs, mammary tissue, ovaries, testes, uterus, seminal vesiclesHistology: mammary gland, ovary, prostate, testes, uterus
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	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 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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	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.
	Metric 8:	Consistency of Exposure Administration	High	Test substance was delivered consistently across study groups.
	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 (7hr/day, 5 day/week for 2 years)
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	Only one concentration was studied, this was based off the current US occupational standard.
	Metric 12:	Exposure Route and Method	Medium	Dynamic whole body was used with 12 air changes/hr.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Animal characteristics were adequately described.
	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 acceptable (50/sex/group).
Domain 5: Outcome Assessment				
	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.

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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):	Reproductive/Developmental
Reported Health Effect(s):	Examine: accessory sex organs, mammary tissue, ovaries, testes, uterus, seminal vesiclesHistology: mammary gland, ovary, prostate, testes, uterus
Duration:	Chronic (>91 days) 2 year
Chemical:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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.

Overall Quality Determination High

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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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				
	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 experimental 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).

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 Animals				
	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 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: Confounding / Variable Control				
	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.
	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

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor initiation assay: Skin, lung, stomach tumors
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				
	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 experimental 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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor initiation assay: Skin, lung, stomach tumors
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 Animals				
	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 Assessment				
	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 exposure 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 groups.
Domain 6: Confounding / Variable Control				
	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.
	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 were used, which is the least appropriate for statistical analysis.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor initiation assay: Skin, lung, stomach tumors
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

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):	Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;
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 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 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).

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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 Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;
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				
	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				

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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 Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;
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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights; Nutritional/Metabolic: Body weights;
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 Outcome(s):	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
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 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).

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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 Outcome(s):	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 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	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.; 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

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Health Outcome(s):	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 13:	Test Animal Characteristics	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.
	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).

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Health Outcome(s):	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 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.

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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 Outcome(s):	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 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.
	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.

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Health Outcome(s):	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 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 Control				
	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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Health Outcome(s):	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 23:	Data Presentation and Analysis	N/A	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).; 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 groups).

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Health Outcome(s):	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

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Health Outcome(s):	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
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 Outcome(s):	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").;
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 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 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				

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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 Outcome(s):	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").;
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:	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 Assessment				
	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. 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 study period.; 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: Confounding / Variable Control				
	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 analyses were not performed/ not necessary (clearly negative findings across groups).

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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 Outcome(s):	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").;
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.

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 Outcome(s):	Mortality; Mortality; Mortality; Mortality;
Reported Health Effect(s):	Mortality: Mortality; Mortality: Mortality; Mortality: Mortality; Mortality: Mortality;
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 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 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).

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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 Outcome(s):	Mortality; Mortality; Mortality; Mortality;
Reported Health Effect(s):	Mortality: Mortality; Mortality: Mortality; Mortality: Mortality; Mortality: Mortality;
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	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).

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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 Outcome(s):	Mortality; Mortality; Mortality; Mortality;
Reported Health Effect(s):	Mortality: Mortality; Mortality: Mortality; Mortality: Mortality; Mortality: Mortality;
Duration:	Chronic (>91 days) 17 weeks - rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	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 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: Confounding / Variable Control				
	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:	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):	Immune/Hematological; Immune/Hematological; Immune/Hematological;
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

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:	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 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).

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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 Outcome(s):	Immune/Hematological; Immune/Hematological; Immune/Hematological;
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

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 Outcome(s):	Immune/Hematological; Immune/Hematological; Immune/Hematological;
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

Domain	Metric		Rating	Comments
Domain 5: Outcome Assessment				
	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: Confounding / Variable Control				
	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

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):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
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 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:	Test Substance Purity	High	The purity of 1,2-dichloroethane was > 99%.
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 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.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights
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:	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 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: Confounding / Variable Control				
	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 Outcome(s):	Hepatic/Liver; Renal/Kidney; Immune/Hematological;
Reported Health Effect(s):	Hepatic/Liver: Related clinical chemistry (Bilirubin measurements); Renal/Kidney: Related clinical chemistry (BUN, electrolytes); Urinalysis; Immune/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 Substance				
	Metric 1:	Test Substance Identity	Medium	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				
	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 Characterization				
	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:	Exposure Frequency and Duration	Medium	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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Study Citation:	IRFMN, (1976). Clinical chemistry results after 6 months inhalatory exposure to ethylene dichloride.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Immune/Hematological;
Reported Health Effect(s):	Hepatic/Liver: Related clinical chemistry (Bilirubin measurements); Renal/Kidney: Related clinical chemistry (BUN, electrolytes); Urinalysis; Immune/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 4: Test Animals				
	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 Assessment				
	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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: body weight changes, food/water intake, and respiratory rates were not reported. The test substance is considered to be a respiratory irritant.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	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.

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Study Citation:	IRFMN, (1976). Clinical chemistry results after 6 months inhalatory exposure to ethylene dichloride.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Immune/Hematological;
Reported Health Effect(s):	Hepatic/Liver: Related clinical chemistry (Bilirubin measurements); Renal/Kidney: Related clinical chemistry (BUN, electrolytes); Urinalysis; Immune/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 Outcome(s):	Immune/Hematological; Hepatic/Liver; Renal/Kidney;
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, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.;
Duration:	Chronic (>91 days) 12-Months
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5447364

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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	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 Characterization				
	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				

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Study Citation:	IRFMN, (1978). Clinical chemistry results in adult rats exposed to ethylene dichloride by inhalation for 12 months.
Health Outcome(s):	Immune/Hematological; Hepatic/Liver; Renal/Kidney;
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, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.;
Duration:	Chronic (>91 days) 12-Months
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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.

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Study Citation:	IRFMN, (1978). Clinical chemistry results in adult rats exposed to ethylene dichloride by inhalation for 12 months.
Health Outcome(s):	Immune/Hematological; Hepatic/Liver; Renal/Kidney;
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, IP, uric acid; urinary pH, proteins, ketone bodies, glucose and bilirubin, casts, crystals, hemoglobin.;
Duration:	Chronic (>91 days) 12-Months
Chemical:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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**

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health 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
Domain 1: Test Substance				
	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 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 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 Administration	High	Water was available ad libitum across groups
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health 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 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 Animals				
	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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health 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

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence
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
Domain 1: Test Substance				
	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 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 Administration	High	Water was available ad libitum across groups
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence
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 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 Animals				
	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 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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence
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

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; water intake
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 Substance				
	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 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 Administration	High	Water was available ad libitum across groups
	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				

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; water intake
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 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 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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	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 reports a statistically 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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; water intake
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

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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 Substance				
	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 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 Administration	High	Water was available ad libitum across groups
	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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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		**High**	

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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Non-cancer lesions; liver weights
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 Substance				
	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 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 Administration	High	Water was available ad libitum across groups
	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				

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Non-cancer lesions; liver weights
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 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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Non-cancer lesions; liver weights
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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 Substance				
	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 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 Animals				
	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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 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: Confounding / Variable Control				
	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

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 Outcome(s):	Neurological/Behavioral; Ocular/Sensory; Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Gastrointestinal; Immune/Hematological; Endocrine (Endocrine); Adipose (Adipose); Reproductive/Developmental;
Reported Health Effect(s):	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;
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 Substance				
	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 Characterization				
	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 Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported.
	Metric 9:	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.; Adipose (Adipose): 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 Outcome(s):	Neurological/Behavioral; Ocular/Sensory; Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Gastrointestinal; Immune/Hematological; Endocrine (Endocrine); Adipose (Adipose); Reproductive/Developmental;
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) 78 weeks- rats
Chemical:	1,1-Dichloroethane- 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 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 Animals				
	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).
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcomes assessment methodology addressed the intended outcomes of 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: Confounding / Variable Control				
	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 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	Medium	All Outcomes: Outcomes with negative findings are reported as such in the text.

Overall Quality Determination Medium

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumors
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 Substance				
	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 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 Animals				
	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				

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumors
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 Control				
	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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 Substance				
	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 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 Animals				
	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				
	Metric 16:	Outcome Assessment Methodology	High	Outcomes assessment methodology addressed the intended outcomes of interest.

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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 19:	Blinding of Assessors	N/A	Not necessary.
	Metric 20:	Negative Control Response	High	Negative control group response was appropriate.
Domain 6: Confounding / Variable Control				
	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

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 Outcome(s):	Neurological/Behavioral; Ocular/Sensory; Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Gastrointestinal; Immune/Hematological; Endocrine (Endocrine); Adipose (Adipose); Reproductive/Developmental;
Reported Health Effect(s):	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;
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 Substance				
	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	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 Characterization				
	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 Administration	Low	All Outcomes: Details of exposure administration are insufficiently reported.
	Metric 9:	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 Animals				
	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 Outcome(s):	Neurological/Behavioral; Ocular/Sensory; Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Gastrointestinal; Immune/Hematological; Endocrine (Endocrine); Adipose (Adipose); Reproductive/Developmental;
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) 78 weeks- mice
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	94773

Domain	Metric		Rating	Comments
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcomes assessment methodology addressed the intended outcomes of 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: Confounding / Variable Control				
	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 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	Medium	All Outcomes: Outcomes with negative findings are reported as such in the text.

Overall Quality Determination Medium

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumors
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 Substance				
	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 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 Animals				
	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				

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumors
Duration:	Chronic (>91 days) 78 weeks- mice
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	High	Negative control group response was appropriate.
Domain 6: Confounding / Variable Control				
	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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; body length
Duration:	Chronic (>91 days) 6 months; dogs
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	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				
	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 guideline 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				
	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)

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weights; body length
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 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: Confounding / Variable Control				
	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

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Survival
Duration:	Chronic (>91 days) 6 months; dogs
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	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				
	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 guideline 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				
	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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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Survival
Duration:	Chronic (>91 days) 6 months; dogs
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1973131

Domain	Metric		Rating	Comments
Domain 5: Outcome 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: Confounding / Variable Control				
	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 Quality Determination Low

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health Effect(s):	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
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 Characterization				
	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				
	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.

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health Effect(s):	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.

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health Effect(s):	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 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.
	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: Confounding / Variable 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	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.

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Cardiovascular; Lung/Respiratory; Immune/Hematological; Endocrine (Endocrine (thyroid, parathyroid, Pancreas, Adrenal); Reproductive/Developmental (Endocrine (thyroid, parathyroid, Pancreas, Adrenal);
Reported Health Effect(s):	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 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**

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Survival
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	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				
	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				
	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 Animals				
	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

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Survival
Duration:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1973131

Domain	Metric		Rating	Comments
Domain 5: Outcome 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: Confounding / Variable Control				
	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

Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Kidney weights and histopathology; serum BUN
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	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				
	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				
	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 Animals				
	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

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Kidney weights and histopathology; serum BUN
Duration:	Chronic (>91 days) 6 months; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	1973131

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: Confounding / Variable Control				
	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 mid-study), 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 Outcome(s):	Reproductive/Developmental; Lung/Respiratory; Hepatic/Liver; Immune/Hematological; Cardiovascular; Lung/Respiratory; Endocrine;
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: 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				
	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?

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Reproductive/Developmental; Lung/Respiratory; Hepatic/Liver; Immune/Hematological; Cardiovascular; Lung/Respiratory; Endocrine;
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: 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 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.
	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 Animals				
	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 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

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Study Citation:	Mellon Institute, (1947). Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons.
Health Outcome(s):	Reproductive/Developmental; Lung/Respiratory; Hepatic/Liver; Immune/Hematological; Cardiovascular; Lung/Respiratory; Endocrine;
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: 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 / Variable 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 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

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 Outcome(s):	Immune/Hematological; Nutritional/Metabolic;
Reported Health Effect(s):	Immune/Hematological: Hematology; Nutritional/Metabolic: Body weight and food intake;
Duration:	Chronic (>91 days) 2 years
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200497

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 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 Characterization				
	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 Administration	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	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				
	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 Assessment				
	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.

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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.
Health Outcome(s):	Immune/Hematological; Nutritional/Metabolic;
Reported Health Effect(s):	Immune/Hematological: Hematology; Nutritional/Metabolic: Body weight and food intake;
Duration:	Chronic (>91 days) 2 years
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 Control				
	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 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

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 Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Lung weight and histology
Duration:	Chronic (>91 days) 2 years
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200497

Domain	Metric		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	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 Design				
	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				
	Metric 7:	Preparation and Storage of Test Substance	Low	There were deficiencies in preparation and storage conditions of test substances.
	Metric 8:	Consistency of Exposure Administration	High	Exposure was administered consistently across study groups.
	Metric 9:	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 Dose/Concentration Spacing	High	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	Whole body chambers were used with 12 +/-1 air changes/hour.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	All test animal characteristics were reported.
	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 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.

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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.
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Lung weight and histology
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 Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant therefore respiratory rate should be 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	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

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 Outcome(s):	Cancer/Carcinogenesis; Mortality;
Reported Health Effect(s):	Cancer/Carcinogenesis: Macroscopic and microscopic lesions were assessed.; Mortality: Mortality;
Duration:	Chronic (>91 days) 2 years
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200497

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 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 Characterization				
	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 Administration	High	All Outcomes: Exposure was administered consistently across study groups.
	Metric 9:	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				
	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 Assessment				
	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.

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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.
Health Outcome(s):	Cancer/Carcinogenesis; Mortality;
Reported Health Effect(s):	Cancer/Carcinogenesis: Macroscopic and microscopic lesions were assessed.; Mortality: Mortality;
Duration:	Chronic (>91 days) 2 years
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200497

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.
Domain 6: Confounding / Variable Control				
	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 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)

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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Histology
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				
	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 Characterization				
	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.

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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 Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Histology
Duration:	Chronic (>91 days) 78 weeks; Mice
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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: 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: Confounding / Variable 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 (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

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Cardiovascular; Thyroid; Hepatic/Liver; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine); Gastrointestinal; Cancer/Carcinogenesis (Endocrine);
Reported Health Effect(s):	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;
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				
	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 Characterization				
	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	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 weeksat 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

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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 Outcome(s):	Cardiovascular; Thyroid; Hepatic/Liver; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine); Gastrointestinal; Cancer/Carcinogenesis (Endocrine);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) 78 weeks; Mice
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5441108

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 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	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.
Domain 6: Confounding / Variable Control				

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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 Outcome(s):	Cardiovascular; Thyroid; Hepatic/Liver; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine); Gastrointestinal; Cancer/Carcinogenesis (Endocrine);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) 78 weeks; Mice
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5441108

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
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				
	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 Characterization				
	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	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
Duration:	Chronic (>91 days) 78 weeks; Mice
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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: 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	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: Confounding / Variable 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 (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

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Histology
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				
	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 Characterization				
	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	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	Dosing administration/frequency was generally 5 days/week, 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.

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Histology
Duration:	Chronic (>91 days) 78 weeks; Mice
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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: 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 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: Confounding / Variable 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 (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

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Mortality; Renal/Kidney;
Reported Health Effect(s):	Mortality: Survival; Renal/Kidney: Histology;
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				
	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 Characterization				
	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				

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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 Outcome(s):	Mortality; Renal/Kidney;
Reported Health Effect(s):	Mortality: Survival; Renal/Kidney: Histology;
Duration:	Chronic (>91 days) 78 weeks; Mice
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 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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Mortality; Renal/Kidney;
Reported Health Effect(s):	Mortality: Survival; Renal/Kidney: Histology;
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

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Behavior, signs of toxic effects, histopathological analysis of the nervous system
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				
	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 Characterization				
	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	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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Behavior, signs of toxic effects, histopathological analysis of the nervous system
Duration:	Chronic (>91 days) 78 weeks; Mice
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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: Outcome Assessment				
	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:	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. 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: Confounding / Variable 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 (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

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Cardiovascular; Cancer/Carcinogenesis; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	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 Substance				
	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 Characterization				
	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				

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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 Outcome(s):	Cardiovascular; Cancer/Carcinogenesis; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	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
	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: Confounding / Variable Control				
	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

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Mortality; Thyroid;
Reported Health Effect(s):	Mortality: Survival; Thyroid: 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 Substance				
	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 Characterization				
	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				

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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 Outcome(s):	Mortality; Thyroid;
Reported Health Effect(s):	Mortality: Survival; Thyroid: Histology;
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 Assessment				
	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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Mortality; Thyroid;
Reported Health Effect(s):	Mortality: Survival; Thyroid: Histology;
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

Study Citation:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
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 Substance				
	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 Characterization				
	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 were not reported.
	Metric 9:	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				

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
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	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	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: Confounding / Variable 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 (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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Bodyweight, food consumption
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:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Renal/Kidney; Reproductive/Developmental; Lung/Respiratory;
Reported Health Effect(s):	Renal/Kidney: Histology; Reproductive/Developmental: Histology; Lung/Respiratory: 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 Substance				
	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 Characterization				
	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				

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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 Outcome(s):	Renal/Kidney; Reproductive/Developmental; Lung/Respiratory;
Reported Health Effect(s):	Renal/Kidney: Histology; Reproductive/Developmental: Histology; Lung/Respiratory: Histology;
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 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	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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Renal/Kidney; Reproductive/Developmental; Lung/Respiratory;
Reported Health Effect(s):	Renal/Kidney: Histology; Reproductive/Developmental: Histology; Lung/Respiratory: Histology;
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:	NTP (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 55:1-103.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Behavior, signs of toxic effects, histopathological analysis of the nervous system
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 Substance				
	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 Characterization				
	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 were not reported.
	Metric 9:	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				

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Behavior, signs of toxic effects, histopathological analysis of the nervous system
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	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: Confounding / Variable 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 (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 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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Behavior, signs of toxic effects, histopathological analysis of the nervous system
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:	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 Outcome(s):	Mortality (This form is for rats)
Reported Health Effect(s):	Death
Duration:	Chronic (>91 days) Chronic; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Design				
	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 Outcome(s):	Mortality (This form is for rats)
Reported Health Effect(s):	Death
Duration:	Chronic (>91 days) Chronic; rats
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 (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				
	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 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.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.

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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 Outcome(s):	Mortality (This form is for rats)
Reported Health Effect(s):	Death
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 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 Outcome(s):	Hepatic/Liver (This form is for rats)
Reported Health Effect(s):	Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol
Duration:	Chronic (>91 days) Chronic; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Design				
	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 Outcome(s):	Hepatic/Liver (This form is for rats)
Reported Health Effect(s):	Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol
Duration:	Chronic (>91 days) Chronic; rats
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 (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				
	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 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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.

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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 Outcome(s):	Hepatic/Liver (This form is for rats)
Reported Health Effect(s):	Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol
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 Medium

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Health Outcome(s):	Lung/Respiratory (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; 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 Substance				
	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 Design				
	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 Outcome(s):	Lung/Respiratory (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; 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 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				
	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 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	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: Confounding / Variable Control				
	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.

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Health Outcome(s):	Lung/Respiratory (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; 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	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

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Health Outcome(s):	Lung/Respiratory (This form is for rats)
Reported Health Effect(s):	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
Domain 1: Test Substance				
	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 Design				
	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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Health Outcome(s):	Lung/Respiratory (This form is for rats)
Reported Health Effect(s):	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 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				
	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 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	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: Confounding / Variable Control				
	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.

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Health Outcome(s):	Lung/Respiratory (This form is for rats)
Reported Health Effect(s):	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	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 Outcome(s):	Immune/Hematological (This form is for Guinea pigs)
Reported Health Effect(s):	Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.
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				
	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 Design				
	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. 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)

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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 Outcome(s):	Immune/Hematological (This form is for Guinea pigs)
Reported Health Effect(s):	Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.
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 Animals				
	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 Assessment				
	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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.

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Health Outcome(s):	Immune/Hematological (This form is for Guinea pigs)
Reported Health Effect(s):	Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.
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 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 Outcome(s):	Nutritional/Metabolic (This form is for Guinea pigs)
Reported Health Effect(s):	Body weight; food consumption
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				
	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 Design				
	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, 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 Outcome(s):	Nutritional/Metabolic (This form is for Guinea pigs)
Reported Health Effect(s):	Body weight; food consumption
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 (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				
	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 Assessment				
	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 / Variable Control				
	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.

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Health Outcome(s):	Nutritional/Metabolic (This form is for Guinea pigs)
Reported Health Effect(s):	Body weight; food consumption
Duration:	Chronic (>91 days) Chronic; Guinea pigs
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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 Medium

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Health Outcome(s):	Renal/Kidney (This form is for Guinea pig); Renal/Kidney (This form is for rats);
Reported Health Effect(s):	Renal/Kidney (This form is for Guinea pig): Gross examinations; histology; organ weights; Renal/Kidney (This form is for rats): Gross examinations; 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 Substance				
	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	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 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	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 Outcome(s):	Renal/Kidney (This form is for Guinea pig); Renal/Kidney (This form is for rats);
Reported Health Effect(s):	Renal/Kidney (This form is for Guinea pig): Gross examinations; histology; organ weights; Renal/Kidney (This form is for rats): Gross examinations; 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 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 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				
	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.

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Health Outcome(s):	Renal/Kidney (This form is for Guinea pig); Renal/Kidney (This form is for rats);
Reported Health Effect(s):	Renal/Kidney (This form is for Guinea pig): Gross examinations; histology; organ weights; Renal/Kidney (This form is for rats): Gross examinations; 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 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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	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.

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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 Outcome(s):	Renal/Kidney (This form is for Guinea pig); Renal/Kidney (This form is for rats);
Reported Health Effect(s):	Renal/Kidney (This form is for Guinea pig): Gross examinations; histology; organ weights; Renal/Kidney (This form is for rats): Gross examinations; 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 Medium

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Health Outcome(s):	Nutritional/Metabolic (This form is for rats)
Reported Health Effect(s):	Body weight; food consumption
Duration:	Chronic (>91 days) Chronic; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Design				
	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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Health Outcome(s):	Nutritional/Metabolic (This form is for rats)
Reported Health Effect(s):	Body weight; food consumption
Duration:	Chronic (>91 days) Chronic; rats
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 (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				
	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 Assessment				
	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 / Variable Control				
	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.

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Health Outcome(s):	Nutritional/Metabolic (This form is for rats)
Reported Health Effect(s):	Body weight; food consumption
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 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 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 Outcome(s):	Cardiovascular (This form is for rats)
Reported Health Effect(s):	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
Domain 1: Test Substance				
	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 Design				
	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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Health Outcome(s):	Cardiovascular (This form is for rats)
Reported Health Effect(s):	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 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				
	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 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	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	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 / Variable Control				
	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.

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Health Outcome(s):	Cardiovascular (This form is for rats)
Reported Health Effect(s):	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	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 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 Outcome(s):	Cardiovascular (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; 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 Substance				
	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 Design				
	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 ≥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 Outcome(s):	Cardiovascular (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; 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 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.
Domain 4: Test Animals				
	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 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 8/sex/group; this is lower than the recommended 20/sex/group is considered appropriate for a chronic study in rodents.
Domain 5: Outcome 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	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.
Domain 6: Confounding / Variable Control				
	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

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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 Outcome(s):	Cardiovascular (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; 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	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, 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 Outcome(s):	Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) Chronic; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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	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 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	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 Outcome(s):	Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) Chronic; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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.

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Health Outcome(s):	Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) Chronic; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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 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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	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.

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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 Outcome(s):	Reproductive/Developmental (This form is for rats); Reproductive/Developmental (This form is for Guinea pigs);
Reported Health Effect(s):	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;
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

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 Outcome(s):	Immune/Hematological (This form is for rats)
Reported Health Effect(s):	Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.
Duration:	Chronic (>91 days) Chronic; rats
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Design				
	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 Outcome(s):	Immune/Hematological (This form is for rats)
Reported Health Effect(s):	Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.
Duration:	Chronic (>91 days) Chronic; rats
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 Animals				
	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 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 / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	No confounding variables were reported.

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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 Outcome(s):	Immune/Hematological (This form is for rats)
Reported Health Effect(s):	Spleen: Gross examinations; histology; organ weights. Lymph node tissues examined.
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

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 Outcome(s):	Hepatic/Liver (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol
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				
	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 Design				
	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, 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				

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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 Outcome(s):	Hepatic/Liver (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol
Duration:	Chronic (>91 days) Chronic; Guinea pigs
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
	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	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	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" 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 and Procedures	Medium	No confounding variables were reported.

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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 Outcome(s):	Hepatic/Liver (This form is for Guinea pigs)
Reported Health Effect(s):	Gross examinations; histology; organ weights; liver lipid analysis; free and esterified cholesterol
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 Outcome(s):	Neurological/Behavioral (This form is for Guinea pigs); Neurological/Behavioral (This form is for Rats);
Reported Health Effect(s):	Neurological/Behavioral (This form is for Guinea pigs): Clinical signs; Neurological/Behavioral (This form is for Rats): Clinical signs;
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				
	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	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 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	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.
	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	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.
	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 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.

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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 Outcome(s):	Neurological/Behavioral (This form is for Guinea pigs); Neurological/Behavioral (This form is for Rats);
Reported Health Effect(s):	Neurological/Behavioral (This form is for Guinea pigs): Clinical signs; Neurological/Behavioral (This form is for Rats): Clinical signs;
Duration:	Chronic (>91 days) Chronic; Guinea pigs
Chemical:	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 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 Assessment				
	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 Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.

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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 Outcome(s):	Neurological/Behavioral (This form is for Guinea pigs); Neurological/Behavioral (This form is for Rats);
Reported Health Effect(s):	Neurological/Behavioral (This form is for Guinea pigs): Clinical signs; Neurological/Behavioral (This form is for Rats): Clinical signs;
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

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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical signs
Duration:	Chronic (>91 days) Chronic; Monkey
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Design				
	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 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.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical signs
Duration:	Chronic (>91 days) Chronic; Monkey
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 4: Test Animals				
	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 Assessment				
	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: Confounding / Variable Control				
	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 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	The text indicates that T-tests were performed comparing exposed groups to air-exposed or unexposed controls whre relevant.

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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 Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Clinical signs
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:	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 Outcome(s):	Neurological/Behavioral (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Nutritional/Metabolic (This form is for 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 Effect(s):	Neurological/Behavioral (This form is for Rabbits): Clinical signs; Reproductive/Developmental (This form is for Rabbits): Testes: Gross examinations; histology; organ weights; Nutritional/Metabolic (This form is for Rabbits): Body weight; food consumption; Immune/Hematological (This form is for 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
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 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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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 Outcome(s):	Neurological/Behavioral (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Nutritional/Metabolic (This form is for 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 Effect(s):	Neurological/Behavioral (This form is for Rabbits): Clinical signs; Reproductive/Developmental (This form is for Rabbits): Testes: Gross examinations; histology; organ weights; Nutritional/Metabolic (This form is for Rabbits): Body weight; food consumption; Immune/Hematological (This form is for 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
HERO ID:	62617

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 Animals				
	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.
Domain 5: Outcome Assessment				
	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	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.

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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 Outcome(s):	Neurological/Behavioral (This form is for Rabbits); Reproductive/Developmental (This form is for Rabbits); Nutritional/Metabolic (This form is for 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 Effect(s):	Neurological/Behavioral (This form is for Rabbits): Clinical signs; Reproductive/Developmental (This form is for Rabbits): Testes: Gross examinations; histology; organ weights; Nutritional/Metabolic (This form is for Rabbits): Body weight; food consumption; Immune/Hematological (This form is for 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
HERO ID:	62617

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.
	Metric 22: 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

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 Outcome(s):	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);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) Chronic; Monkey
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 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: 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.

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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 Outcome(s):	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);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) Chronic; Monkey
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	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				
	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 Assessment				
	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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	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

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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 Outcome(s):	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);
Reported Health Effect(s):	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;
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

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 Outcome(s):	Cardiovascular (This form is for Monkey); Lung/Respiratory (This form is for Monkey); Reproductive/Developmental (This form is for Monkey);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) Chronic; Monkey
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62617

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 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: 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.

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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 Outcome(s):	Cardiovascular (This form is for Monkey); Lung/Respiratory (This form is for Monkey); Reproductive/Developmental (This form is for Monkey);
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) Chronic; Monkey
Chemical:	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 Animals				
	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 Assessment				
	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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: No confounding variables were reported.
	Metric 22:	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 Quality Determination Uninformative

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence (examination of thymus and isolation of individual masses)
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 Substance				
	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 Characterization				
	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				

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence (examination of thymus and isolation of individual masses)
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 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	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: Confounding / Variable 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 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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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence (examination of thymus and isolation of individual masses)
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**	

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence (examination of thymus and isolation of individual masses)
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 Substance				
	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 Characterization				
	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	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 Animals				
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor incidence (examination of thymus and isolation of individual masses)
Duration:	Chronic (>91 days) 40 weeks-Males
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200612

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: Confounding / Variable 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 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

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 Outcome(s):	Immune/Hematological; Immune/Hematological;
Reported Health Effect(s):	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
Domain 1: Test Substance				
	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%.
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	Immune/Hematological: A positive control was not needed for this study.; Immune/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.
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 Animals				
	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.

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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 Outcome(s):	Immune/Hematological; Immune/Hematological;
Reported Health Effect(s):	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 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 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 and 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 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. 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: Confounding / Variable Control				
	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	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.; Immune/Hematological: 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	Immune/Hematological: Statistical methods were adequately described.; Immune/Hematological: Statistical analyses was described appropriately

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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 Outcome(s):	Immune/Hematological; Immune/Hematological;
Reported Health Effect(s):	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

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 Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Changes to body weight; Nutritional/Metabolic: Changes to body weight;
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 Substance				
	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 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	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 Animals				
	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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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 Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Nutritional/Metabolic: Changes to body weight; Nutritional/Metabolic: Changes to body weight;
Duration:	Chronic (>91 days) 40 weeks-Males
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200612

Domain	Metric		Rating	Comments
Domain 5: Outcome 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: Confounding / Variable Control				
	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	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 Outcome(s):	Missing 'other' target organ; Missing 'other' target organ;
Reported Health Effect(s):	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;
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 Substance				
	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 Design				
	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 transgenic mice. Carcinogenesis 16(2):285-293.
Health Outcome(s):	Missing 'other' target organ; Missing 'other' target organ;
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) 40 weeks-Males
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200612

Domain		Metric	Rating	Comments
Domain 4: Test Animals				
	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 substantial 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 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	All Outcomes: The number of animals was appropriate.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The choice of tissue to evaluate for changes to histopathology and the 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 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	Medium	All Outcomes: Gross necropsy was only performed on mice that were had died or were 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' target organ: Blinding of assessors was not needed
	Metric 20:	Negative Control Response	Low	All Outcomes: The responses of the negative control were not reported.
Domain 6: Confounding / Variable Control				
	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	All Outcomes: There was no information either to support or dismiss any differences among groups in animal attrition or health outcomes unrelated to exposure.

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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 Outcome(s):	Missing 'other' target organ; Missing 'other' target organ;
Reported Health Effect(s):	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;
Duration:	Chronic (>91 days) 40 weeks-Males
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200612

Domain	Metric		Rating	Comments
	Metric 23:	Data Presentation 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 Data	Uninformative	All Outcomes: Data from serum biochemistry and gross necropsy was not reported in the text or figures.

Overall Quality Determination Uninformative

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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: Survival; Mortality: Survival;
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 Substance				
	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 Design				
	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 Animals				
	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				

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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 Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: Survival; Mortality: Survival;
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 level of lymphoma observed in transgenic PIM mice.
Domain 6: Confounding / Variable Control				
	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:	Data Presentation and Analysis	High	All Outcomes: Statistical analyses were adequately described.
	Metric 24:	Reporting of Data	High	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

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
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	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 Characterization				
	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

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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 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 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	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 Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology and the assessment methodology were sensitive and appropriate.

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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 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 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: Confounding / Variable Control				
	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.

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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

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):	Lung/Respiratory; Endocrine (Endocrine);
Reported Health Effect(s):	Lung/Respiratory: Lung weights (mean and relative to body weight) were determined; nasal cavity, trachea, and lung were evaluated for histopathology; 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
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 Substance	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 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).; 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 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	Lung/Respiratory: Administered doses/concentrations were reported without ambiguity; Endocrine (Endocrine): Administered doses/concentrations were reported without ambiguity.
	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 Dose/Concentration Spacing	Low	All Outcomes: Only one dose of 1,2-dichloroethane was tested; effects were observed (no NOAEL)

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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 Outcome(s):	Lung/Respiratory; Endocrine (Endocrine);
Reported Health Effect(s):	Lung/Respiratory: Lung weights (mean and relative to body weight) were determined; nasal cavity, trachea, and lung were evaluated for histopathology; 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 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	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	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.
	Metric 15:	Number of Animals per Group	Low	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.
Domain 5: Outcome Assessment				
	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.

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Health Outcome(s):	Lung/Respiratory; Endocrine (Endocrine);
Reported Health Effect(s):	Lung/Respiratory: Lung weights (mean and relative to body weight) were determined; nasal cavity, trachea, and lung were evaluated for histopathology; 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: Confounding / Variable Control				
	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
HERO ID:	4451542

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 Characterization				
	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)

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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
HERO ID:	4451542

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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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
HERO ID:	4451542

Domain	Metric		Rating	Comments
	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 Assessment				
	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	All Outcomes: Adequate sampling was used.
	Metric 19:	Blinding of Assessors	N/A	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: Blinding is not applicable for study type

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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
HERO ID:	4451542

Domain	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 changes were reported in Table 3.; Immune/Hematological: The biological responses of the negative control groups were adequate. No histopathological changes/differences were noted between treated versus control animals.
Domain 6: Confounding / Variable Control				
	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.

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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 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
HERO ID:	4451542

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.; Urinary (Urinary): 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.

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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 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
HERO ID:	4451542

Domain	Metric	Rating	Comments
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):	Musculoskeletal
Reported Health Effect(s):	Skeletal muscle was evaluated for histopathology
Duration:	Chronic (>91 days) 26 weeks
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	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				
	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
Domain 3: Exposure Characterization				
	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				
	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.

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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 Outcome(s):	Musculoskeletal
Reported Health Effect(s):	Skeletal muscle was 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 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: Confounding / Variable 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 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.

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):	Nutritional/Metabolic
Reported Health Effect(s):	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
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	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				
	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 3: Exposure Characterization				
	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				
	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.

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	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
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4451542

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: Confounding / Variable 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 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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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):	Nutritional/Metabolic
Reported Health Effect(s):	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
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	4451542

Domain	Metric	Rating	Comments
Overall Quality Determination		**High**	

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):	Mortality
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
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 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.

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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):	Mortality
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
HERO ID:	194588

Domain	Metric		Rating	Comments
	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.
	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 repeated (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 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 (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 Outcome(s):	Mortality
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
HERO ID:	194588

Domain	Metric		Rating	Comments
	Metric 16:	Outcome Assessment Methodology	High	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, 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: 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	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 — Uninformative

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):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: serum urea, uric acid, glucose; Hepatic/Liver: liver fat content, serum total protein, cholesterol, ALT, AST;
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	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 Characterization				
	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.

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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):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: serum urea, uric acid, glucose; Hepatic/Liver: liver fat content, serum total protein, cholesterol, ALT, AST;
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 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 monitoring of the test substance residues.

Domain 4: Test 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):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: serum urea, uric acid, glucose; Hepatic/Liver: liver fat content, serum total protein, cholesterol, ALT, AST;
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 Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: 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	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: Confounding / Variable Control				
	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.

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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):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: serum urea, uric acid, glucose; Hepatic/Liver: liver fat content, serum total protein, cholesterol, ALT, AST;
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

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):	Reproductive/Developmental
Reported Health Effect(s):	fertility (no. mated, no. pregnant, no. with litters), litter size, litter survival, litter weights
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.
	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 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.

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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):	Reproductive/Developmental
Reported Health Effect(s):	fertility (no. mated, no. pregnant, no. with litters), litter size, litter survival, litter weights
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 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 Animals				
	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.

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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):	Reproductive/Developmental
Reported Health Effect(s):	fertility (no. mated, no. pregnant, no. with litters), litter size, litter survival, litter weights
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 6: 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 development in mice. Toxicology and Applied Pharmacology 63(3):409-421.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fertility, gestation, viability, litter size, sex ratio, pup weight gain and teratology
Duration:	Reproductive/Developmental multigenerational- 1,2-Dichloroethane
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	62609

Domain	Metric		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	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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	Preparation and storage conditions of test substance was adequate.
	Metric 8:	Consistency of Exposure Administration	High	Exposure was consistent across study groups
	Metric 9:	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				
	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.

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fertility, gestation, viability, litter size, sex ratio, pup weight gain and teratology
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_2007 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 Control				
	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.
	Metric 23:	Data Presentation and Analysis	High	Statistics analysis were performed and appropriate.
	Metric 24:	Reporting of Data	High	All outcome data was reported.

Overall Quality Determination High

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 Outcome(s):	Mortality; Nutritional/Metabolic;
Reported Health 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
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 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				
	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 Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Preparation and storage conditions of test substance was adequate.
	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 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 Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and doses administered were appropriate 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				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Initial body weights were not provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group were appropriate for outcomes studied.
Domain 5: Outcome Assessment				
	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.

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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 Outcome(s):	Mortality; Nutritional/Metabolic;
Reported Health 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: Confounding / Variable Control				
	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

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Maternal body weights
Duration:	Reproductive/Developmental GD 6-20- inhalation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	12099

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Maternal body weights
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 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: Confounding / Variable Control				
	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 ± 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 Outcome(s):	Mortality
Reported Health Effect(s):	Maternal death (GD 6-20 oral and inhalation)
Duration:	Reproductive/Developmental GD 6-20- inhalation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	12099

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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 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 Outcome(s):	Mortality
Reported Health Effect(s):	Maternal death (GD 6-20 oral and inhalation)
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 Assessment				
	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: Confounding / Variable Control				
	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 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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Maternal toxicity, pregnancy outcomes and fetal external, skeletal, and visceral examinations (oral and inhalation, GD6-20)
Duration:	Reproductive/Developmental GD 6-20- inhalation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	12099

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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	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				

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Maternal toxicity, pregnancy outcomes and fetal external, skeletal, and visceral examinations (oral and inhalation, GD6-20)
Duration:	Reproductive/Developmental GD 6-20- inhalation
Chemical:	1,1-Dichloroethane- 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, 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 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	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 / Variable Control				
	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 ± SEM where appropriate. Individual animal data were not provided in this published report.

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 Outcome(s):	Mortality
Reported Health Effect(s):	Maternal death (GD 6-20 oral and inhalation)
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				
	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 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				

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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 Outcome(s):	Mortality
Reported Health Effect(s):	Maternal death (GD 6-20 oral and inhalation)
Duration:	Reproductive/Developmental GD6-20 - oral
Chemical:	1,1-Dichloroethane- 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 Assessment				
	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: Confounding / Variable Control				
	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 1,2-dichloroethane in rats. Toxicological Sciences 28(2):187-198.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Maternal body weights
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				
	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 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 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	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	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				

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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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Maternal body weights
Duration:	Reproductive/Developmental GD6-20 - oral
Chemical:	1,1-Dichloroethane- 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 Assessment				
	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	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 measures.
	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	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 dataset.
	Metric 24:	Reporting of Data	High	The data for each exposure group were quantitatively reported as means ± 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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Maternal toxicity, pregnancy outcomes and fetal external, skeletal, and visceral examinations (oral and inhalation, GD6-20)
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				
	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 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 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	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.

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Maternal toxicity, pregnancy outcomes and fetal external, skeletal, and visceral examinations (oral and inhalation, GD6-20)
Duration:	Reproductive/Developmental GD6-20 - oral
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	12099

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				
	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 Assessment				
	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 / Variable Control				
	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 ± SEM.

Overall Quality Determination — 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.
Health Outcome(s):	Mortality; Reproductive/Developmental;
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 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	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				
	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 Animals				
	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.

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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.
Health Outcome(s):	Mortality; Reproductive/Developmental;
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: Confounding / Variable Control				
	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**

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 Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight, food consumption
Duration:	Reproductive/Developmental Developmental
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5453539

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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 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 Animals				
	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 Assessment				
	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.

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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.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Body weight, food consumption
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: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	Test substance is a respiratory irritant and therefore respiratory rate should be 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	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., 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 Outcome(s):	Mortality; Reproductive/Developmental;
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 Reproduction
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5453539

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 Characterization				
	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, 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 Animals				
	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.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methodologies were appropriate.

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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.
Health Outcome(s):	Mortality; Reproductive/Developmental;
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 Reproduction
Chemical:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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	High	Mortality: Mortality was reported.; Reproductive/Developmental: Data were sufficiently reported.

Overall Quality Determination Medium

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 Outcome(s):	Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic;
Reported Health Effect(s):	Renal/Kidney: Repro study: Kidney weight, histology; Hepatic/Liver: Repro study: Liver weight, histology; Nutritional/Metabolic: Body weight, food consumption;
Duration:	Reproductive/Developmental Reproduction
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5453539

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 Characterization				
	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, 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 Animals				
	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.
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.

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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.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Nutritional/Metabolic;
Reported Health Effect(s):	Renal/Kidney: Repro study: Kidney weight, histology; Hepatic/Liver: Repro study: Liver weight, histology; Nutritional/Metabolic: Body weight, food consumption;
Duration:	Reproductive/Developmental Reproduction
Chemical:	1,1-Dichloroethane- 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: Confounding / Variable Control				
	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 sialodacryoadenitis 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 Outcome(s):	Neurological/Behavioral
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
Domain 1: Test Substance				
	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 Characterization				
	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.

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Study Citation:	WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.
Health Outcome(s):	Neurological/Behavioral
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 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.
	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.
Domain 4: Test Animals				
	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 guidelines, which specifies using enough mating pairs to obtain at least 20 litters.
Domain 5: Outcome 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. Histopathology was performed for high-dose and control groups only, but no effects were observed at the high dose.
	Metric 19:	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				

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Study Citation:	WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.
Health Outcome(s):	Neurological/Behavioral
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 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 Outcome(s):	Clinical signs (Clinical Signs)
Reported Health Effect(s):	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
Duration:	Reproductive/Developmental Extended 1-generation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	7310776

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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 Characterization				
	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.

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Study Citation:	WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.
Health Outcome(s):	Clinical signs (Clinical Signs)
Reported Health Effect(s):	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
Duration:	Reproductive/Developmental Extended 1-generation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	7310776

Domain	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.
Domain 4: Test Animals				
	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 guidelines, which specifies using enough mating pairs to obtain at least 20 litters.
Domain 5: Outcome 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.
Domain 6: Confounding / Variable Control				
	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.

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Domain	Metric		Rating	Comments
	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 reporting incidences and sample size and individual animal data were provided.

Overall Quality Determination — Uninformative

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Health Outcome(s):	Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;
Reported Health Effect(s):	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
Domain 1: Test Substance				
	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%.
Domain 2: Test Design				
	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.
Domain 3: Exposure Characterization				
	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.

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Reported Health Effect(s):	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 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.

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Duration:	Reproductive/Developmental Extended 1-generation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	7310776

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

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Reported Health Effect(s):	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 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				

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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.

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Duration:	Reproductive/Developmental Extended 1-generation
Chemical:	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.

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Study Citation:	WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.
Health Outcome(s):	Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;
Reported Health Effect(s):	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 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.

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Health Outcome(s):	Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;
Reported Health Effect(s):	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 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 subjective in nature.; Cardiovascular: Blinding is not required because the outcome(s) are not subjective in nature.; Musculoskeletal: Blinding is not required because the outcome(s) are not subjective in nature.

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Reported Health Effect(s):	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 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.

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Reported Health Effect(s):	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
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Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			

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Domain	Metric		Rating	Comments
	Metric 21:	Confounding Variables in Test Design and Procedures	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

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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.

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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

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Study Citation:	WIL Research, (2015). An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats.
Health Outcome(s):	Mortality; Endocrine (Endocrine); Nutritional/Metabolic; Immune/Hematological; Hepatic/Liver; Renal/Kidney; Thyroid; Lung/Respiratory; Gastrointestinal; Ocular/Sensory; Reproductive/Developmental; Cardiovascular; Musculoskeletal;
Reported Health Effect(s):	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
Overall Quality Determination		**Uninformative**	

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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	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
Duration:	Reproductive/Developmental Rats- 5 weeks
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	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 Substance	Low	The preparation and storage of test substance were not reported.
	Metric 8:	Consistency of Exposure Administration	Low	Details on exposure administration are insufficiently reported.
	Metric 9:	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 Animals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights and age 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	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.
	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.

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	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
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: 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 differences 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 Uninformative

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 Outcome(s):	Nutritional/Metabolic; Hepatic/Liver; Immune/Hematological; Renal/Kidney;
Reported Health Effect(s):	Nutritional/Metabolic: Body weight of pregnant rats (5 weeks); Hepatic/Liver: Serum ALT (GPT) and AST (GOT) for pregnant rat (5 weeks); Immune/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
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified 1,2-dichloroethane.
	Metric 2:	Test Substance Source	Low	All Outcomes: The source of the test substance was Beijing Chemical Plant Two. Batch/lot number was not provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: The purity of test substance was reported as 98.5%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Low	All Outcomes: It is not clear if the animals were untreated or sham exposed.
	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 does not report how animals were allocated.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: The preparation and storage of test substance were not reported.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: Details on exposure administration are insufficiently reported.
	Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: Actual concentrations were reported, however the analytical method used to make these measurements was not reported.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency was appropriate (6 hrs/day).
	Metric 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).
	Metric 12:	Exposure Route and Method	Uninformative	All Outcomes: There is no description of the inhalation chamber.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Starting body weights and age 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	Low	All Outcomes: The number of animals/group was not reported.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Nutritional/Metabolic: Details on methodology were not reported.; Hepatic/Liver: Serum ALT and AST were evaluated. No histology or liver weight.; Immune/Hematological: Details on which parameters assessed were not reported.; Renal/Kidney: Only urinary protein was evaluated.
	Metric 17:	Consistency of Outcome Assessment	Low	All Outcomes: There were no details regarding the execution of the study protocol.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: Details regarding sampling of outcomes were not reported.

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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 Outcome(s):	Nutritional/Metabolic; Hepatic/Liver; Immune/Hematological; Renal/Kidney;
Reported Health Effect(s):	Nutritional/Metabolic: Body weight of pregnant rats (5 weeks); Hepatic/Liver: Serum ALT (GPT) and AST (GOT) for pregnant rat (5 weeks); Immune/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: Confounding / Variable Control				
	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 Uninformative

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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	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
Duration:	Reproductive/Developmental Mice- GD9-GD10
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 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				
	Metric 7:	Preparation and Storage of Test Substance	Low	The preparation and storage of test substance were not reported.
	Metric 8:	Consistency of Exposure Administration	Low	Details on exposure administration are insufficiently reported.
	Metric 9:	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 Dose/Concentration Spacing	Low	Only one concentration studied. No data are reported to evaluate responses.
	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 Husbandry Conditions	Low	Husbandry conditions were not reported.
	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.

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	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
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 differences 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 Uninformative

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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	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
Duration:	Reproductive/Developmental Mice- GD6-GD15
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	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 Substance	Low	The preparation and storage of test substance were not reported.
	Metric 8:	Consistency of Exposure Administration	Low	Details on exposure administration are insufficiently reported.
	Metric 9:	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 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 Animals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights and age 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	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.
	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.

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	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
Duration:	Reproductive/Developmental Mice- GD6-GD15
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 differences unrelated to exposure.
	Metric 23: Data Presentation and Analysis	Low	Statistical analysis was performed but not described adequately.
	Metric 24: Reporting of Data	Low	Some results are reported in text of results. Not adequately reported.

Overall Quality Determination **Uninformative**

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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	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
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 test"
	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 Substance	Low	The preparation and storage of test substance were not reported.
	Metric 8:	Consistency of Exposure Administration	Low	Details on exposure administration are insufficiently reported.
	Metric 9:	Reporting of Doses/Concentrations	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 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 Animals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights and age 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	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.

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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 Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	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
Duration:	Reproductive/Developmental Male rats- 7 days
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200708

Domain	Metric		Rating	Comments
	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	High	The negative control responses were reported and appropriate.
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 differences unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	Low	Statistical analysis was performed but not described adequately.
	Metric 24:	Reporting of Data	High	Data were reported for outcomes.

Overall Quality Determination Uninformative

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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor initiation assay: Skin, lung, stomach tumors
Duration:	Other (specify) Single Dose Tumor Initiator.
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	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.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation (in acetone) was 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	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor initiation assay: Skin, lung, stomach tumors
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 Animals				
	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 Assessment				
	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 data table indicates that (for a list of chemicals), the ”duration of the test and median survival times 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 the untreated 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: Confounding / Variable Control				
	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.

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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 Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Tumor initiation assay: Skin, lung, stomach tumors
Duration:	Other (specify) Single Dose Tumor Initiator.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	94473

Domain	Metric	Rating	Comments
	Metric 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.
	Metric 24: Reporting 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 Uninformative

Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.
Health Outcome(s):	Irritation (eye irritation)
Reported Health Effect(s):	Eye irritation (signs of redness and chemosis); skin irritation (signs of erythema, edema, or corrosiveness)
Duration:	Other (specify) Acute - Eye irritation
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	6569955

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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.
Domain 3: Exposure Characterization				
	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 Administration	High	Available information suggests all animals received the same treatment.
	Metric 9:	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 Assessment				

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Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.
Health Outcome(s):	Irritation (eye irritation)
Reported Health Effect(s):	Eye irritation (signs of redness and chemosis); skin irritation (signs of erythema, edema, or corrosiveness)
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 Control				
	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 Outcome(s):	Irritation (Skin irritation)
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
HERO ID:	6569955

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	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				
	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				
	Metric 7:	Preparation and Storage of Test Substance	Low	No information on preparation was provided.
	Metric 8:	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 undera 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.
Domain 4: Test Animals				
	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.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment (Draize method) was appropriate for the study type.

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Study Citation:	Stauffer Chemical Company, (1973). Acute oral toxicity and eye and skin irritation properties of ethylene dichloride.
Health Outcome(s):	Irritation (Skin irritation)
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
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: Confounding / Variable Control				
	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	High	Individual animal scores at each timepoint were reported.

Overall Quality Determination Medium