40 CFR Part 799

[OPTS-42059E; FRL 3634-6]

Testing Consent Order for 1,1,1-Trichloroethane and Response to the Interagency Testing Committee

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This rule announces that EPA has signed an enforceable testing consent order with five manufacturers of 1,1,1-trichloroethane (TCEA) (CAS No. 71-55-6), who have agreed to perform mutagenicity and neurotoxicity tests with TCEA. TCEA is added to the list of Testing Consent Orders in 40 CFR 799.5000 for which the export notification requirements of 40 CFR part 707 apply. This rule constitutes an additional EPA response to the Interagency Testing Committee's (ITC) recommendation that EPA consider health effects testing of TCEA. In October 1984, EPA issued a final Phase I test rule requiring that manufacturers perform a developmental toxicity test with TCEA.

EFFECTIVE DATE: August 23, 1989.

FOR FURTHER INFORMATION CONTACT: Michael M. Stahl, Director, Environmental Assistance Division (TS-799), Office of Toxic Substances, Room EB-44, 401 M Street SW., Washington, DC 20460, (202) 554-1404. TDD (202) 554-0551.

SUPPLEMENTARY INFORMATION: Under procedures described in 40 CFR part 790, The Dow Chemical Company, ICI Americas, Inc., Vulcan Chemicals, Occidental Chemical Corp., and PPG Industries, Inc., (the Companies) have entered into a Testing Consent Order with EPA in which these companies have agreed to perform mutagenicity and neurotoxicity testing of TCEA. This rule amends subpart C of 40 CFR part 799 to add TCEA to the list of chemical substances and mixtures subject to testing consent orders.

I. ITC Recommendation

In its Second Report to EPA, published in the **Federal Register** of April 19, 1978 (43 FR 16684), the ITC recommended that TCEA be considered for health effects testing.

In the **Federal Register** of October 10, 1984 (49 FR 39810), EPA issued a final phase I rule requiring manufacturers and processors of TCEA to perform a developmental toxicity test. The Agency deferred inclusion of mutagenicity and neurotoxicity testing because the tiered testing scheme for mutagenicity testing and the neurotoxicity test guidelines had not been sufficiently developed. Both the test scheme and guidelines are now available, the EPA is, therefore, requiring that this testing be performed.

II. Testing Consent Order Negotiations

In the **Federal Register** of August 20, 1987 (52 FR 31445), and in accordance with the procedures established in 40 CFR 790.28, EPA requested persons

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interested in participating in or monitoring testing negotiations on TCEA to contact the Agency. EPA held public meetings with interested parties on September 10 and October 29, 1987; August 4 and November 28 through 29, 1988; and February 3, 1989, to discuss the testing appropriate for TCEA. In July and August 1989, five TCEA manufacturers and EPA signed a Testing Consent Order for TCEA. Under the Order, the manufacturers agreed to conduct or provide for the conduct of an in vivo mammalian cytogenetics micronucleus assay, a rodent dominant lethal test (if triggered), and six neurotoxicity tests: Functional observational battery (acute and subchronic), sensory evoked potential battery (acute and subchronic), neuropathology, and a developmental neurotoxicity screen. The specific test standards to be followed and the testing schedule for each test were included in the Order. Procedures for submitting study plans, modifying the Order, monitoring the testing and other provisions were also included in the Order.

III. Use and Exposure

The final phase I test rule on TCEA issued on October 10, 1984, was issued under section 4(a)(1)(B) of TSCA. In that rule, EPA found that TCEA was produced in substantial quantities and there was substantial occupational and consumer exposure to TCEA resulting from its manufacture, processing, and use. The bases for the findings were presented in the final rule and the support document for the rule (Ref. 1). Additional information is now available which further documents the extent of consumer and general population exposure to TCEA (Refs. 2 through 4).

It is also worth noting that TCEA, because of its contribution to chlorine in the stratosphere, is under review for possible inclusion in future revisions to the Montreal Protocol on Substances That Deplete the Ozone Layer (April 17, 1989; 54 FR 15228). Although it is not now clear what controls the Parties to the Protocol will agree to, TCEA will continue to be used to some extent in the near future. In addition, due to the physicial and chemical properties of TCEA and its predominant use as an expendable solvent, even a major reduction in production volume would still result in substantial human exposure. Residual amounts of TCEA will remain in the environment contributing to human exposure and supporting the need for these data. Therefore, the tests specified in this consent order remain essential.

IV. Testing Program

A. Mutagenicity

The mutagenicity potential of TCEA and the limitations of the available studies have been adequately reviewed in EPA's "Health Assessment Document for 1,1,1-Trichloroethane (Methyl Chloroform)" (Ref. 5) and in EPA's support document for the phase I test rule for TCEA (Ref. 1). In brief, TCEA is mutagenic in *Salmonella typhimurium* strains TA 1535, TA 1537, and TA 100 both with and without metabolic activation (Refs. 6 and 7). In addition, in the *Drosophila* sex-linked recessive lethal study sponsored by EPA, TCEA was reported to induce recessive lethal mutations in spermatocytes when administered by feeding (Ref. 8). However, although there is some indication that TCEA may induce lethal mutations in this *Drosophila* study, the data indicate at most a weak response and are insufficient in themselves to warrant proposing that the mouse visible specific locus test be required at this time (Ref. 9).

Concerning chromosomal effects, three in vivo cytogenetics tests have been conducted with TCEA (Refs. 10 through 12). These tests, however, were not conducted well enough to evaluate the potential of TCEA to cause chromosomal effects. In the studies by Cocke et al. (Ref. 10) and Tsuchimoto and Matter (Ref. 11), the bone marrow was harvested too soon (only 6 hours) after the last dose. In the study by Salamone (Ref. 12), only male mice were tested. A dominant lethal test has also been conducted with TCEA as part of a two-generation fertility study in mice (Ref. 13). Statistically significant differences were reported in the ratio of dead to live fetuses; however, both increases and decreases were observed. This screening level study was judged to be inadequate because animals were not given doses high enough to produce overt signs of toxicity and because there is uncertainty over the dose the animals actually received (Ref. 5). In addition, the purity of the TCEA (96 percent TCEA, 3 percent dioxane) and route of administration (oral) are not comparable to the test substance and route specified in this Order. Other mutagenicity studies that have been identified and reviewed by EPA (Refs. 1 and 5) have been judged inadequate because conventional protocols were used that did not adjust test conditions and procedures to accommodate TCEA's high volatility and low water solubility; controls were not included in the experimental design; and/or too few animals were used in the study to provide adequate data.

The available studies are inadequate to fully characterize and evaluate the potential of TCEA to cause chromosomal effects.

Under the Consent Order, the Companies have agreed to a tiered testing program. The first tier test is a micronucleus test to be conducted according to an HSIA protocol. EPA has accepted this alternative methodology because it believes the test will provide reliable and adequate data equal to that which would be obtained from testing according to the TSCA guideline. The second tier test is the dominant lethal test which shall be conducted according to the TSCA guideline. The tests agreed upon are presented in IV.B. below.

B. Neurotoxicity

TCEA has been shown to produce non-specific central nervous system (CNS) depression in humans after exposure to doses ranging from 500 through 2,650 ppm (Refs. 14 through 17). Only one of these studies (Ref. 16) had an exposure duration of more than 1 day. In this study, CNS depression was observed after exposure to 500 ppm for 7 hours/day for 5 days. The other three studies utilized short-term exposures which varied from a few minutes to several hours. None of the studies were adequate to characterize either short- or long-term neurologic effects of exposure to TCEA. Of particular note, CNS effects were noted for the 5-day exposure to ppm TCEA (Ref. 16) but not for the 7[illegible] minute exposure (Ref. 15) to this concentration, suggesting that exposure longer than 5 days may cause CNS effects at even lower concentations. In addition, 350 to 550 ppm TCEA have been shown to impair perceptual speed, manual dexterity and reaction time (Refs. 18 and 19).

A number of neuropathological and behavioral disorders are associated with chronic exposure to organic solvents such as TCEA. The effects noted in workers exposed to solvents include: decreased concentration ability, memory, learning ability, impulse control, and motivation; emotional instability; and impaired peripheral nerve function (Refs. 20 and 21). These disorders (referred to as solvent syndrome) can persist for years after cessation of exposure and may be irreversible. In addition, EPA has been informed of neurological problems (CNS depression, reoccurring loss of motor activity, and loss of memory) in workers exposed to TCEA (Refs. 22 and 23). Although these reports are anecdotal, they further support EPA's concern for the effects of TCEA on the nervous system.

Available animal studies of TCEA's effects on the nervous system and behavior are summarized in reference 5. Effects reported were on motor activity, vestibular control, and fixed-interval response rate. However, the endpoints measured in these studies were evaluated in only a preliminary manner and no-effect levels were not determined. Although these studies further support concern for the neurotoxicity potential of TCEA, they are inadequate to fully characterize the acute and chronic neurotoxic potential of TCEA, especially behavioral and developmental neurotoxicity effects. No adequate studies on the potential of TCEA to cause neurophysiological, neuropathological, or neurobehavioral effects were identified.

In the Consent Order, the Companies agreed to conduct six neurotoxicity tests with TCEA, and systems development and positive control verification of the developmental neurotoxicity test. These six tests will be conducted according to protocols submitted by HSIA, and approved by EPA. EPA has agreed to testing by these protocols because it believes that they will provide equally reliable and adequate data to evaluate the neurotoxic effects of TCEA. Some of these tests may provide better data than the current TSCA guidelines but EPA cannot determine this until the data have been thoroughly evaluated. The tests agreed upon are presented in the following table.

TABLE—TESTING PLAN FOR TCEA

	Test methods	Report date [1]
Tier 1 tests:		
Functional observational battery, acute and subchronic	HSIA Protocol [2, 3]	21
Sensory evoked potential battery, acute and subchronic	HSIA Protocol [2, 3]	21
Neuropathology, subchronic	HSIA Protocol [2]	21
Systems development and positive control verification of developmental neurotoxicity test.	See Appendix 3	[4] 18
Developmental neurotoxicity test	HSIA Protocol [5]	36
Micronucleus test	HSIA Protocol [6]	14
Tier 2 test: Dominant lethal [7]	40 CFR 798.5450	24

[1] Number of months after the effective date of the Consent Order when the final test results must be submitted to EPA.
[2] Halogenated Solvents Industry Alliance (HSIA) Protocol entitled "Acute Motor Activity and Neurophysiologic Effects of 1,1,1-Trichloroethane in Rats", Appendix 1 to the Consent Order.
[3] HSIA Protocol entitled "Neurotoxicologic Examination of Rats Exposed to 1,1,1-Trichloroethane Vapor for 13 weeks", Appendix 2 to the Consent Order.
[4] An unaudited draft report will be submitted for review at this time. A final report will be prepared concurrently with the developmental neurotoxicity test of TCEA.
[5] HSIA Protocol entitled "Examination of Rats for Developmental Neurotoxicologic Effects from Maternal Exposure to 1,1,1-Trichloroethane", Appendix 4 to the Consent Order.
[6] HSIA Protocol entitled "An Inhalation Mouse Bone Marrow Micronucleus Test on 1,1,1-Trichloroethane", Appendix 5 to the Consent Order.
[7] This test must be conducted only if EPA notifies the Companies.

In this consent agreement, EPA has approved the use of test protocols specifically developed to evaluate the mutagenic and neurotoxic potential of TCEA. The data generated by these tests will be used to determine the risk of mutagenic and neurotoxic effects associated with the manufacture, processing, use, and disposal of TCEA. Until the results of the testing required by this consent order have been fully evaluated by EPA, EPA will probably not consider using these methods for neurotoxicity and mutagenicity testing in any other consent order under TSCA section 4.

V. Export Notification

In addition to the Phase I test rule, the issuance of the Consent Order subjects any person who exports or intends to export TCEA to the export notification requirements of section 12(b) of TSCA. The specific requirements are listed in 40 CFR part 707. In the June 30, 1986 (51 FR 23706), Interim Rule establishing the Testing Consent Order process, EPA added and reserved subpart C of part 799 for listing of testing consent orders issued by EPA. This listing serves as notification to persons, who export or intend to export chemical substances or mixtures which are the subject of testing consent orders, that 40 CFR part 707 applies.

VI. Rulemaking Record

EPA has established a record for this rule and the Consent Order (docket number OPTS-42059E). This record contains the basic information considered by EPA in developing this rule and the Testing Consent Order. This record includes the following information:

A. Supporting Documentation

(1) Testing Consent Order between five TCEA manufacturers and the EPA.

(2) Federal Register notices pertaining to this rule and consent order consisting of:

(a) Notice of final rule on EPA's TSCA Good Laboratory Practice Standards (48 FR 53922; November 29, 1983).

(b) Notice of interim final rule on procedures governing Testing Consent Agreements and Test Rules and Exemption Procedures (51 FR 23706; June 30, 1986).

(c) Toxic Substances Control Act Test Guidelines; Final Rules (50 FR 39252; September 27, 1985).

(d) Notice of final rule revising the Toxic Substances Control Act Test Guidelines (52 FR 19056; May 20, 1987).

(e) Notice containing the ITC recommendation of TCEA to the Priority List (43 FR 16684; April 19, 1978).

(f) Notice of proposed test rule for 1,1,1-trichloroethane (46 FR 30300; June 5, 1981).

(g) Notice of final Phase I test rule for 1,1,1-trichloroethane (49 FR 39810; October 10, 1984).

(h) Notice of final Phase II test rule for 1,1,1-trichloroethane (50 FR 51683; December 19, 1985).

(i) Notice of proposed test rule for triethylene glycol monomethyl, monoethyl, and monobutyl ethers (51 FR 17883; May 15, 1986).

(j) Notice soliciting interested parties for developing a consent order for 1,1,1-trichloroethane (52 FR 31445; August 20, 1987).

B. References

(1) USEPA. U.S. Environmental Protection Agency. Assessment of Testing Needs: 1,1,1-Trichloroethane. Office of Pesticides and Toxic Substances. USEPA. Washington, DC. (May 1981).

(2) USEPA. Household Products Containing Methylene Chloride and Other Chlorinated Solvents: "A Shelf Survey." Office of Toxic Substances, USEPA. Washington, DC. (July 1987). (EPA 560/5-87-006).

(3) USEPA. Household Solvent Products: A National Usage Survey. Office of Toxic Substances, USEPA. Washington, DC. (July 1987). (EPA 560/5-87-005).

(4) Versar Inc., Springfield, VA. Physical-Chemical Properties, Environmental Fate and Mobility, and Monitoring Data for Six Halogenated Solvents. Prepared for the

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Office of Toxic Substances, USEPA, Washington, DC. (July 1987).

(5) USEPA. Health Assessment Document for 1,1,1-Trichloroethane (Methyl Chloroform). Office of Health and Environmental Assessment. USEPA. Washington, DC (February 1984).

(6) Margard, W. "Summary report on in vitro biassay of chlorinated hydrocarbon solvents to Detrex Chemical Industries, Inc." Battelle Columbus Laboratories, Inc. Columbus, OH. (July 31, 1978).

(7) Simmon, V. F., Kauhanen, K., and Tardiff, R. G. "Mutagenic activity of chemicals identified in drinking water." *Developmental Toxicology and Environmental Science*. 2:249–258. (1977).

(8) USEPA. "*Drosophila* sex-linked recessive lethal assay of 1,1,1-trichloroethane." Genetic Bioassay Branch, Health Effects Research Laboratory. USEPA. Research Triangle Park, NC. (April 26, 1985).

(9) USEPA. "1,1,1-Trichloroethane (TCEA): Review of *Drosophila* Sex-linked Recessive Lethal Assay." Intra-agency memorandum from Micheal Cimino, Toxic Effects Branch to Frank Benenati, Test Rules Development Branch, Office of Toxic Substances, Washington, DC 20460. (June 30, 1987).

(10) Gocke, E., King, M. T., Eckhardt, K., and Wild, D. "Mutagenicity of cosmetics ingredients licensed by European Communities." *Mutation Research*. 90:91–109. (1981).

(11) Tsuchimoto, T. and Matter, B. E. "Activity of coded compounds in the micronucleus test." In: "Evaluation of short term tests for carcinogens. Report of the international collaborative study." *Progress in Mutation Research*. Volume 1. de Serres, F. and Ashby, J., eds. Amsterdam: Elsevier, pp. 705–11. (1981).

(12) Salamone, M. F., Heddle, J. A., and Katz, M. "Mutagenic activity of 41 compounds in the in vivo micronucleus assay." In: "Evaluation of short term tests for carcinogens. Report of the international collaborative study." *Progress in Mutation Research*. Volume 1. de Serres, F. and Ashby, J., eds. Amsterdam: Elsevier, pp. 686–97. (1981).

(13) Lane, R. W., Riddle, B. L., and Borzelleca, J. F. "Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and development in mice." *Toxicology and Applied Pharmacology* 63:409–21. (1982).

(14) Torkelson, T. R., Oyen, F., McCollister, D., and Rowe, V. K. "Toxicity of 1,1,1-trichloroethane as determined on laboratory animals and human subjects." *American Industrial Hygiene Association Journal*. 19:353–362. (1958).

(15) Stewart, R. D., Gay, H. H., Erley, D. S., Hake, C. L., and Schaffer, A. W. "Human exposure to 1,1,1-trichloroethane vapor: Relationship of expired air and blood concentrations to exposure and toxicity." *American Industrial Hygiene Association Journal*. 22:252–262. (1961).

(16) Stewart, R. D., Gay, H. H., Schaffer, A. W., Erley, D. S., and Rowe, V. K. "Experimental human exposure to methyl chloroform vapor." *Archives of Environmental Health*. 19:467–472. (1969).

(17) Dornette, W. H. L. and Jones, J. P. "Clinical experiences with 1,1,1-trichloroethane. A preliminary report of 50 anesthetic administrations." *Anesthesia and Analgesia*. 39:249–253. (1960).

(18) Salvini, M., Binaschi, S., and Riva, M. "Evaluation of the psychophysiological functions in humans exposed to the 'Threshold Limit Value' of 1,1,1-trichloroethane." *British Journal of Industrial Medicine*. 28:286–292. (1971).

(19) Gamberale, F. and Hultengren, M. "Methylchloroform exposure II. Psychophysiological functions." *Work Environmental Health*. 10:82–92. (1973).

(20) National Institute for Occupational Safety and Health. "Organic Solvent Neurotoxicity." Current Intelligence Bulletin 48. Department of Health and Human Services, NIOSH Publication No. 87–104. (March 31, 1987).

(21) World Health Organization/Nordic Council of Ministers Working Group. "Chronic effects of organic solvents on the central nervous system and diagnostic criteria." Copenhagen, Denmark. (June 10–14, 1985).

(22) USEPA. Memorandum to the file on neurotoxicity from exposure to TCEA on naval vessels. Frank Benenati, Test Rules Development Branch, Office of Toxic Substances, USEPA, Washington, DC. (October 8, 1987).

(23) USEPA. Telephone conversation between H. Sacarello, Science Management Corp., and Frank Benenati, Test Rules Development Branch, Office of Toxic Substances, USEPA, Washington, DC. (October 7, 1987).

Confidential Business Information (CBI), while part of the record, is not available for public review. A public version of the record, from which CBI has been deleted, is available for inspection in the OTS Public Information Office, Room NE–G004, 401 M Street, SW., Washington, DC from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays.

VII. Other Regulatory Requirements

The information collection requirements contained in this rule been approved by the Office of Management and Budget (OMB) under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3501 *et seq.* and have been assigned OMB control number 2070–0033.

Public reporting burden for this collection of information is estimated to average 8 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, PM–223, U.S. Environmental Protection Agency, 401 M Street, SW., Washington, DC 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070–0033), Washington, DC 20503.

List of Subjects in 40 CFR Part 799

Chemical export, Chemicals, Environmental protection, Hazardous substances, Recordkeeping and reporting requirements, Testing procedures.

Dated: August 7, 1989.

Charles L. Elkins,

Assistant Administrator for Pesticides and Toxic Substances.

Therefore, 40 CFR part 799 is amended as follows:

PART 799—[AMENDED]

The authority citation continues to read as follows:

Authority: 15 U.S.C. 2603, 2611, 2625.

2. Section 799.5000 is amended by adding the following chemical substance in Chemical Abstract Service (CAS) Registry Number order to the table, to read as follows:

§ 799.5000 Testing consent orders.

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CAS number	Substance or mixture name	Testing	Federal Register citation
71-55-6	1,1,1-Trichloroethane	Health effects	August 23, 1989.

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