EPA-540/1-86-045

Agency

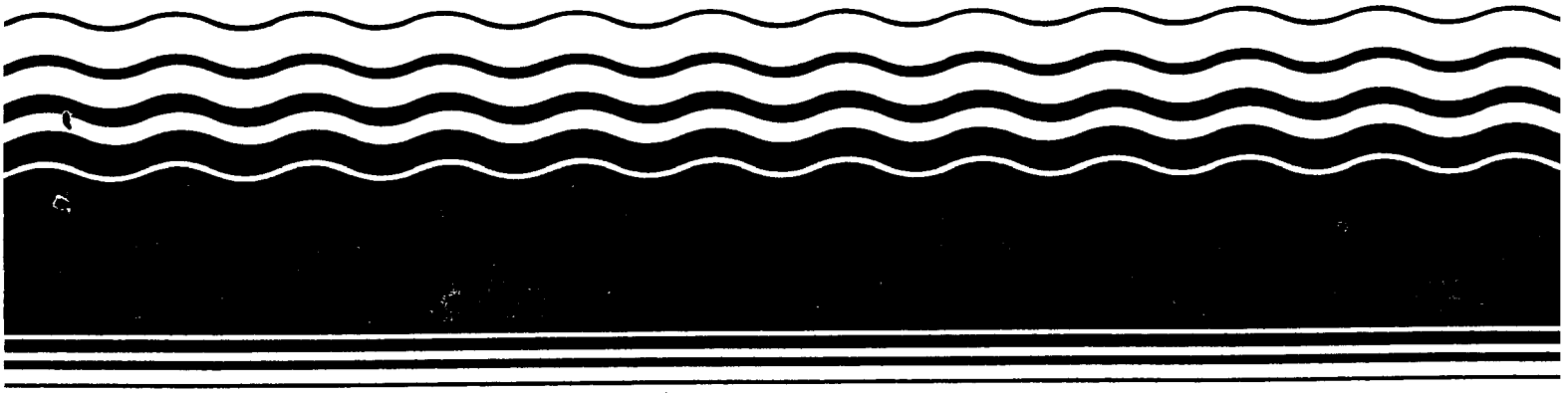
Office of Emergency and
Remedial Response
Washington DC 20460

Office of Research and Development
Office of Health and Environmental
Assessment
Environmental Criteria and
Assessment Office
Cincinnati OH 45268

Superfund

EPA

HEALTH EFFECTS ASSESSMENT FOR 1,1,2-TRICHLOROETHANE



EPA/540/1-86-045
September 1984

HEALTH EFFECTS ASSESSMENT FOR 1,1,2-TRICHLOROETHANE

U.S. Environmental Protection Agency
Office of Research and Development
Office of Health and Environmental Assessment
Environmental Criteria and Assessment Office
Cincinnati, OH 45268

U.S. Environmental Protection Agency
Office of Emergency and Remedial Response
Office of Solid Waste and Emergency Response
Washington, DC 20460

DISCLAIMER

This report has been funded wholly or in part by the United States Environmental Protection Agency under Contract No. 68-03-3112 to Syracuse Research Corporation. It has been subject to the Agency's peer and administrative review, and it has been approved for publication as an EPA document. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with 1,1,2-trichloroethane. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered as preliminary and reflect limited resources allocated to this project. Pertinent toxicologic and environmental data were located through on-line literature searches of the Chemical Abstracts, TOXLINE, CANCERLINE and the CHEMFATE/DATALOG data bases. The basic literature searched supporting this document is current up to September, 1984. Secondary sources of information have also been relied upon in the preparation of this report and represent large-scale health assessment efforts that entail extensive peer and Agency review. The following Office of Health and Environmental Assessment (OHEA) sources have been extensively utilized:

U.S. EPA. 1980b. Ambient Water Quality Criteria for Chlorinated Ethanes. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-029. NTIS PB 81-117400. (Cited in U.S. EPA, 1982)

U.S. EPA. 1982. Hazard Profile on 1,1,2-trichloroethane. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983b. Review of Toxicologic Data in Support of Evaluation for Carcinogenic Potential of: 1,1,2-Trichloroethane. Prepared by the Carcinogen Assessment Group, OHEA, Washington, DC for the Office of Solid Waste and Emergency Response, Washington, DC.

The intent in these assessments is to suggest acceptable exposure levels whenever sufficient data were available. Values were not derived or larger uncertainty factors were employed when the variable data were limited in scope tending to generate conservative (i.e., protective) estimates. Nevertheless, the interim values presented reflect the relative degree of hazard associated with exposure or risk to the chemical(s) addressed.

Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, the AIS or acceptable intake subchronic, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval (i.e., for an interval that does not constitute a significant portion of the lifespan). This type of exposure estimate has not been extensively used or rigorously defined, as previous risk assessment efforts have been primarily directed towards exposures from toxicants in ambient air or water where lifetime exposure is assumed. Animal data used for AIS estimates generally include exposures with durations of 30-90 days. Subchronic human data are rarely available. Reported exposures are usually from chronic occupational exposure situations or from reports of acute accidental exposure.

The AIC, acceptable intake chronic, is similar in concept to the ADI (acceptable daily intake). It is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan [see U.S. EPA (1980a) for a discussion of this concept]. The AIC is route specific and estimates acceptable exposure for a given route with the implicit assumption that exposure by other routes is insignificant.

Composite scores (CSs) for noncarcinogens have also been calculated where data permitted. These values are used for ranking reportable quantities; the methodology for their development is explained in U.S. EPA (1983a).

For compounds for which there is sufficient evidence of carcinogenicity, AIS and AIC values are not derived. For a discussion of risk assessment methodology for carcinogens refer to U.S. EPA (1980a). Since cancer is a process that is not characterized by a threshold, any exposure contributes an increment of risk. Consequently, derivation of AIS and AIC values would be inappropriate. For carcinogens, q_1^*s have been computed based on oral and inhalation data if available.

ABSTRACT

In order to place the risk assessment evaluation in proper context, refer to the preface of this document. The preface outlines limitations applicable to all documents of this series as well as the appropriate interpretation and use of the quantitative estimates presented.

No data are available which address the potential carcinogenicity of this compound in humans. Limited in vitro mutagenicity evaluations have been negative. Only one cancer bioassay has been conducted. In this study 1,1,2-trichloroethane was carcinogenic in mice, but not rats by oral administration. Using the mouse data, a human q_1^* of 5.73×10^{-2} $(mg/kg/day)^{-1}$ was computed.

No data addressing the potential carcinogenicity of this compound by the inhalation route were located.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3112 for EPA's Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa and Karen Blackburn were the Technical Project Monitors and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Emergency and Remedial Response, Washington, DC.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Office of Air Quality Planning and Standards
Office of Solid Waste
Office of Toxic Substances
Office of Drinking Water

Editorial review for the document series was provided by:

Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office
Cincinnati, OH

Technical support services for the document series was provided by:

Bette Zwayer, Pat Daunt, Karen Mann and Jacky Bohanon
Environmental Criteria and Assessment Office
Cincinnati, OH

TABLE OF CONTENTS

TABLE OF CONTENTS (cont.)

LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AIC	Acceptable intake chronic
AIS	Acceptable intake subchronic
BCF	Bioconcentration factor
bw	Body weight
CAS	Chemical Abstract Service
CS	Composite score
ppm	Parts per million
STEL	Short-term exposure limit
TLV	Threshold limit value
TWA	Time-weighted average

1. ENVIRONMENTAL CHEMISTRY AND FATE

The relevant physical and chemical properties and environmental fate of 1,1,2-trichloroethane (CAS No. 79-00-5) are as follows:

Chemical class:	halogenated aliphatic hydrocarbon
Molecular weight:	133.41 (Verschueren, 1983)
Vapor pressure:	30.3 mm Hg at 25°C (Mackay et al., 1982)
Water solubility:	4500 mg/ℓ at 20°C (Verschueren, 1983)
Log octanol/water partition coefficient:	2.38 (Konemann, 1981)
BCF:	21 (estimated from the equation of Veith et al., 1979)
Soil mobility: (predicted as retardation factor for a soil depth of 140 cm and organic carbon content of 0.087%)	<1.5 (Wilson et al., 1981)
Half-lives in	
Air:	24 days (Singh et al., 1981)
Water:	1.9 days (Zoeteman et al., 1980)

The half-life of 1,1,2-trichloroethane in soil could not be located in the available literature; however, volatilization is expected to be the predominant loss mechanism from the soil surface. In subsurface soil, biodegradation of this compound is likely to be a slow process (Wilson et al., 1981). Based on the aqueous solubility and octanol/water partition coefficient, 1,1,2-trichloroethane is expected to leach into groundwater (Page, 1981; Wilson et al., 1981).

2. ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL ANIMALS

2.1. ORAL

Pertinent data regarding the absorption of orally administered 1,1,2-trichloroethane could not be located in the available literature. By analogy to other chlorinated ethanes, 1,1,2-trichloroethane is rapidly absorbed from the gastrointestinal tract (U.S. EPA, 1980b).

2.2. INHALATION

Pertinent data regarding the absorption of inhaled 1,1,2-trichloroethane could not be located in the available literature. By analogy to other chlorinated ethanes, 1,1,2-trichloroethane is rapidly absorbed following inhalation exposure.

3. TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS

3.1. SUBCHRONIC

3.1.1. Oral. Pertinent data regarding the subchronic oral toxicity of 1,1,2-trichloroethane could not be located in the available literature.

3.1.2. Inhalation. In an unpublished Dow Chemical Company study, Torkelson and Rowe (1981) exposed rats, guinea pigs and rabbits (numbers and strains unspecified) to 15 ppm (81.8 mg/m^3) 1,1,2-trichloroethane for 7 hours/day, 5 days/week for 6 months, or to 30 ppm (163.7 mg/m^3) 7 hours/day, 5 days/week for 16 exposures. No effects were noted on organ weight, hematology or clinical chemistry, but fatty changes were observed in female rats at the high dose.

3.2. CHRONIC

3.2.1. Oral. The NCI (1978) administered TWA doses of 46 or 92 mg/kg bw/day to Osborne-Mendel rats and 195 or 390 mg/kg bw/day to B6C3F1 mice (50 animals/species/sex/dose) by gavage, 5 days/week for 78 weeks, followed by a 13-35 week observation period. The corresponding controls consisted of 20 animals each. No dose-related, non-neoplastic changes were reported for either sex of either species.

3.2.2. Inhalation. Pertinent data regarding the chronic inhalation toxicity of 1,1,2-trichloroethane could not be located in the available literature.

3.3. TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS

3.3.1. Oral. Pertinent data regarding the teratogenicity or other reproductive effects of orally administered 1,1,2-trichloroethane could not be located in the available literature.

3.3.2. Inhalation. Pertinent data regarding the teratogenicity or other reproductive effects of inhaled 1,1,2-trichloroethane could not be located in the available literature.

3.4. TOXICANT INTERACTIONS

Traiger and Plaa (1974) reported that pretreatment with acetone or isopropyl alcohol (2.5 mg/kg bw by gavage) resulted in an increased hepatotoxic response to, and enhanced the effects of threshold doses of 1,1,2-trichloroethane in mice.

4. CARCINOGENICITY

4.1. HUMAN DATA

4.1.1. Oral. Pertinent data regarding the oral carcinogenicity of 1,1,2-trichloroethane in humans could not be located in the available literature.

4.1.2. Inhalation. Pertinent data regarding the carcinogenicity of inhaled 1,1,2-trichloroethane in humans could not be located in the available literature.

4.2. BIOASSAYS

4.2.1. Oral. The NCI (1978) treated groups of 50 male and 50 female B6C3F1 mice or Osborne-Mendel rats with 195 or 390 mg/kg bw/day (mice) or 46 or 92 mg/kg bw/day (rats), 5 days/week for 78 weeks by gavage. The mice were observed for an additional 13 weeks and the rats for an additional 35 weeks. There was no relationship between 1,1,2-trichloroethane treatment and the development of tumors in rats. All groups of treated mice had significantly ($p<0.01$) increased incidences of hepatocellular carcinomas. The incidences were 37/49, 18/49, 2/20 and 0/20 (males) and 40/45, 16/48, 0/20 and 2/20 (females) for the high-dose, low-dose, vehicle control and untreated control groups, respectively. The incidence of adrenal pheochromocytomas was increased in the high-dose groups (both sexes).

4.2.2. Inhalation. Pertinent data regarding the carcinogenicity of inhaled 1,1,2-trichloroethane in experimental animals could not be located in the available literature.

4.3. OTHER RELEVANT DATA

1,1,2-trichloroethane has been tested for mutagenicity in the Ames Salmonella typhimurium assay, both by the standard plate incorporation assay and by exposing the cells to vapors of the compound in a closed container (Barber et al., 1981; Simmon et al., 1977). Doses up to 158.9 µmol/plate,

a level toxic to the Salmonella strains used (TA1535, TA100, TA98), produced only negative results, both with and without the addition of rat liver S-9 preparation to provide metabolic activation.

4.4. WEIGHT OF EVIDENCE

Since 1,1,2-trichloroethane has only been demonstrated to induce liver tumors in one strain of mice in one experiment, the evidence for the carcinogenicity of 1,1,2-trichloroethane in animals is best considered "limited". Since no data are available regarding the carcinogenicity of 1,1,2-trichloroethane in humans, the chemical is best classified as a Group C compound - Possible Human Carcinogen, by applying the criteria for weight of evidence proposed by the Carcinogen Assessment Group of the U.S. EPA (Federal Register, 1984).

5. REGULATORY STANDARDS AND CRITERIA

The ACGIH (1980) has established a TLV of 10 ppm (~45 mg/m^3) and a STEL of 20 ppm (~90 mg/m^3), based on "the toxicological resemblance to symmetric tetrachloroethane and by analogy with the TLV for chloroform." The Occupational Safety and Health Administration has adopted this TLV as a general industry standard (Code of Federal Regulations, 1981).

The U.S. EPA (1980b) has estimated that a concentration of 6.0 µg/ℓ in ambient water will result in an excess lifetime cancer risk of 10^{-5}.

6. RISK ASSESSMENT

6.1. ACCEPTABLE INTAKE SUBCHRONIC (AIS)

1,1,2-Trichloroethane is a chemical associated with liver tumors in mice and for which data are sufficient for calculation of a q_1^*. It is, therefore, inappropriate to calculate an oral or inhalation AIS for 1,1,2-trichloroethane.

6.2. ACCEPTABLE INTAKE CHRONIC (AIC)

1,1,2-Trichloroethane is a chemical associated with liver tumors in mice and for which data are sufficient for calculation of a q_1^*. It is, therefore, inappropriate to calculate an oral or inhalation AIC for 1,1,2-trichloroethane.

6.3. CARCINOGENIC POTENCY (q_1^*)

6.3.1. Oral. One study (NCI, 1978) has indicated that 1,1,2-trichloroethane is carcinogenic in B6C3F1 mice (see Section 4.2.1.). The U.S. EPA (1980b) has calculated a human q_1^* of 5.73×10^{-2} $(mg/kg\ bw/day)^{-1}$, based on the incidence of hepatocellular carcinoma in male mice (Table 6-1) and using a linearized multistage model.

6.3.2. Inhalation. Pertinent data regarding the carcinogenicity of 1,1,2-trichloroethane in humans or experimental animals exposed by inhalation could not be located in the available literature.

A complete data set for the derivation of the q_1^* is presented in Appendix B.

TABLE 6-1

Incidence of Hepatocellular Carcinoma in Male B6C3F1 Mice Exposed to 1,1,2-Trichloroethane*

Dose (mg/kg bw/day)	Incidence (No. Responding/No. Tested)
0	2/20
195	18/49
390	37/49

*Source: U.S. EPA, 1980b

7. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values for Substances in Workroom Air, 4th ed. Cincinnati, OH. p. 406. (Cited in U.S. EPA, 1982)

Barber, E.D., W.H. Donish and K.R. Mueller. 1981. A procedure for the quantitative measurement of the mutagenicity of volatile liquids in the Ames Salmonella/microsome assay. J. Mutat. Res. 90(1): 31-48. (Cited in U.S. EPA, 1982)

Code of Federal Regulations. 1981. OSHA Safety and Health Standards. 29 CFR 1910.10000.

Federal Register. 1984. Environmental Protection Agency. Proposed guidelines for carcinogenic risk assessment. 49 FR 46294-46299.

Konemann, H. 1981. Quantitative structure-activity relationships in fish toxicity studies. Part 1: Relationship for 50 industrial pollutants. Toxicology. 19: 209-221.

Mackay, D., A. Babra, D.W. Chan and W.Y. Shiu. 1982. Vapor pressure correlations for low-volatility environmental chemicals. Environ. Sci. Technol. 16: 645-649.

NCI (National Cancer Institute). 1978. Bioassay of 1,1,2-trichloroethane for possible carcinogenicity. U.S. DWEW Tech. Rep. Ser. 74, Washington, DC. Publ. No. NIH 78-1324. (Cited in U.S. EPA, 1983b)

Page, G.W. 1981. Comparison of groundwater and surface water for patterns and levels of contamination by toxic substances. Environ. Sci. Technol. 15: 1475-1481.

Simmon, V.F., K. Kauhanen and R.G. Tardiff. 1977. Mutagenic activity of chemicals identified in drinking water. Toxicol. Environ. Sci. 2: 249-258. (Cited in U.S. EPA, 1980b, 1982)

Singh, H.B., L.J. Salas, A.J. Smith and H. Shigeishi. 1981. Measurements of some potentially hazardous organic chemicals in urban environments. Atmos. Environ. 15: 601-612.

Torkelson, T.R. and V.K. Rowe. 1981. Halogenated aliphatic hydrocarbons: 1,1,2-trichloroethane. In: Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, Inc., New York. p. 3510-3513.

Traiger, G.J. and G.L. Plaa. 1974. Chlorinated hydrocarbon toxicity. Arch. Environ. Health. 28: 276. (Cited in U.S. EPA, 1980b)

U.S. EPA. 1980a. Guidelines and Methodology Used in the Preparation of Health Effects Assessment Chapters of the Consent Decree Water Quality Criteria. Federal Register. 45: 79347-79357.

U.S. EPA. 1980b. Ambient Water Quality Criteria for Chlorinated Ethanes. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-029. NTIS PB 81-117400. (Cited in U.S. EPA, 1982)

U.S. EPA. 1982. Hazard Profile on 1,1,2-trichloroethane. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983a. Methodology and Guidelines for Reportable Quantity Determinations Based on Chronic Toxicity Data. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983b. Review of Toxicologic Data in Suport of Evaluation for Carcinogenic Potential of: 1,1,2-Trichloroethane. Prepared by the Carcinogen Assessment Group, OHEA, Washington, DC for the Office of Solid Waste and Emergency Response, Washington, DC.

Veith, G.D., D.L. DeFoe and B.V. Bergstedt. 1979. Measuring and estimating the bioconcentration factor of chemicals in fish. J. Fish Res. Board Can. 36: 1040-1048.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemistry, 2nd ed. Van Nostrand Reinhold Company, New York. 1310 p.

Wilson, J.T., C.G. Enfield, W.J. Dunlap, R.L. Cosby, D.A. Foster and L.B. Baskin. 1981. Transport and fate of selected organic pollutants in a sandy soil. J. Environ. Qual. 10: 501-506.

Zoeteman, B.C.J., K. Harmsen, J.B.H.J. Linders, C.F.H. Morra and W. Slooff. 1980. Persistent organic pollutants in river water and groundwater of the Netherlands. Chemosphere. 9: 231-249.

APPENDIX A

Summary Table for 1,1,2-Trichloroethane

Carcinogenic Potency	Species	Experimental Dose/Exposure	Effect	q_1^*	Reference
Inhalation				ND	
Oral	mice	0, 195 or 390 mg/kg bw/day	hepatocellular carcinoma	5.73×10^{-2} $(mg/kg/day)^{-1}$	NCI, 1978; U.S. EPA, 1980

ND = Not derived

APPENDIX B

Cancer Data Sheet for Derivation of q_1^*

Compound: 1,1,2-trichloroethane

Reference: NCI, 1978

Species, Strain, Sex: mice, B6C3F1, male

Body weight: 0.33 kg (measured)

Length of exposure (le) = 546 days

Length of experiment (Le) = 637 days

Lifespan of animal (L) = 637 days

Tumor site and type: liver, hepatocellular carcinoma

Route, vehicle: oral, gavage

Experimental Doses or Exposures (mg/kg/day)	Transformed Dose* (mg/kg/day)	Incidence No. Responding/No. Tested or Examined
0	0	2/20
195	119.14	18/49
390	239.143	37/49

*Calculated to reflect treatment on 5 days/week and for 546 days of 637-day experimental period

Unadjusted q_1^* from study = 4.4611191×10^{-3} $(mg/kg/day)^{-1}$

Human q_1^* = 5.73×10^{-3} $(mg/kg/day)^{-1}$