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Environmental Protection 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

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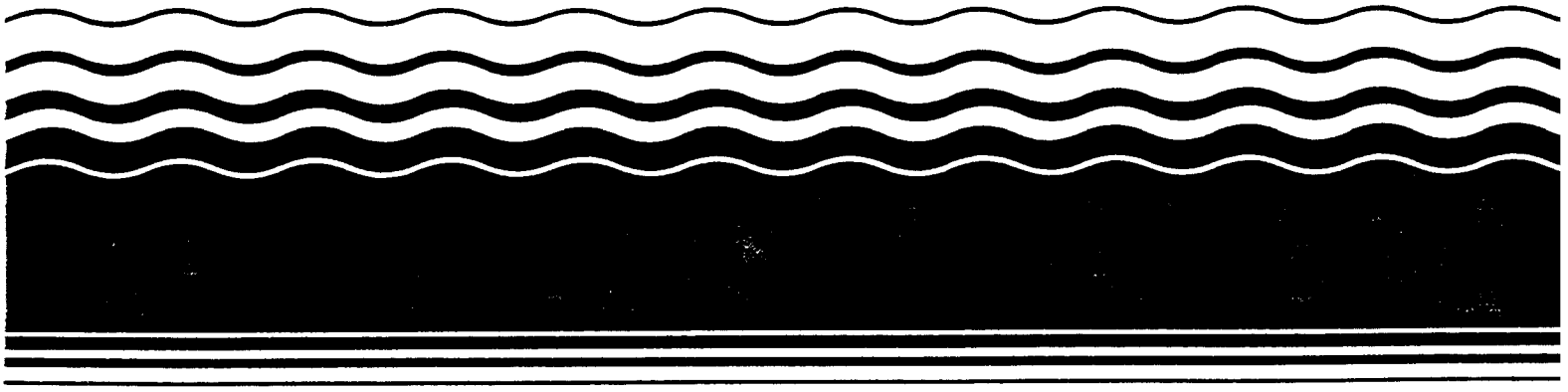
HEALTH EFFECTS ASSESSMENT FOR cis-1,2-DICHLOROETHYLENE



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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 cis-1,2-dichloroethylene. 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) source has been extensively utilized:

U.S. EPA. 1980a. Ambient Water Quality Criteria for Dichloroethylenes. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-041. NTIS PB 81-117525.

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 (1980b) 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 (1983).

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 (1980b). 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.

Data were inadequate to estimate AIS or AIC values for either oral or inhalation routes. Data were also inadequate to assess the carcinogenic potency of this chemical.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AIC	Acceptable intake chronic
AIS	Acceptable intake subchronic
BCF	Bioconcentration factor
CS	Composite score
MFO	Mixed function oxidase
ppm	Parts per million
STEL	Short-term exposure limit
TLV	Threshold limit value

1. ENVIRONMENTAL CHEMISTRY AND FATE

The relevant physical and chemical properties and environmental fate of cis-1,2-dichloroethylene (CAS No. 156-59-2) are given below.

Chemical class:	halogenated aliphatic hydrocarbon
Molecular weight:	96.95
Vapor pressure at 25°C:	208 mm Hg (Torkelson and Rowe, 1981)
Water solubility at 20°C:	3500 mg/ℓ (Torkelson and Rowe, 1981)
Octanol/water partition coefficient:	5 (estimated)
BCF:	0.8 (estimated)
Half-lives in	
Air:	1.3 days (Hendry and Kenly, 1979)
Water:	<1-6 days (estimated)

The octanol/water partition coefficient value for this compound has been estimated from the equation of Kenaga and Goring (1980) and the value of water solubility given above. Similarly, the BCF value has been estimated from the equation of Veith et al. (1979) and the estimated octanol/water partition coefficient value.

The half-life of cis-1,2-dichloroethylene due to its volatilization (the most important loss process) from aquatic media has been estimated as follows: the value for the evaporative half-life for the isomeric compound (i.e., trans-1,2-dichloroethylene) can be estimated to be 1-6 days from the reaeration rate ratio (Mabey et al., 1981) and the oxygen reaeration rate of 0.19-0.96 day^{-1} (Mabey et al., 1981). The volatilization loss of cis-1,2-dichloroethylene from aquatic media was experimentally determined to be slightly higher than its trans-isomer (Tabak et al., 1981). Therefore, the half-life for volatilization of cis-1,2-dichloroethylene has been estimated to be <1-6 days.

Pertinent data regarding the fate of cis-1,2-dichloroethylene in soil could not be located in the available literature. Based on the behavior of the compound in aquatic media, evaporation of cis-1,2-dichloroethylene from the soil surface is expected to be the predominant loss mechanism. In subsurface soil, biodegradation of this compound is likely to be a slow process (Tabak et al., 1981). Therefore, the compound is expected to have the potential to leach from subsurface soil into groundwater. Page (1981) reported cis-1,2-dichloroethylene in groundwaters from New Jersey at a frequency of 44%.

2. ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL MAMMALS

2.1. ORAL EXPOSURE

Pertinent data regarding the oral absorption of cis-1,2-dichloroethylene could not be located in the available literature. The U.S. EPA (1980a) estimates that "virtually 100 percent of ingested DCE may be absorbed systemically," based on the studies of Daniel (1963) and Monster et al. (1976) using trichloroethylene.

2.2. INHALATION

Pertinent data regarding the absorption of cis-1,2-dichloroethylene from the respiratory tract could not be located in the available literature. The U.S. EPA (1980a) estimates that "35 to 50 percent of inhaled DCE...may be absorbed systemically," based on the studies of Daniel (1963) and Monster et al. (1976) using trichloroethylene.

3. TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS

3.1. SUBCHRONIC

3.1.1. Oral. Springer (1965) administered a mixture of cis- and trans-1,2-dichloroethylene to rats for 7 weeks (0.05, 0.25, 0.5 or 1.0 g/kg). It was not clear from the review if these were daily, weekly or total doses. No adverse effects were reported at any dose level. Pertinent data regarding the subchronic oral toxicity of pure cis-1,2-dichloroethylene could not be located in the available literature.

cis-1,2-Dichloroethylene administered to rats as a single dose of either 400 or 1500 mg/kg by gavage in corn oil resulted in increases in a series of hepatic enzymes which are indicators of hepatotoxicity. The authors suggest that cis-1,2-dichloroethylene is a less potent hepatotoxin than 1,1-dichloroethylene. In addition, the cis isomer of 1,2-dichloroethylene appears to be slightly more hepatotoxic than the trans isomer with respect to these endpoints (Jenkins et al., 1972).

3.1.2. Inhalation. Exposure of rats for 8 hours to trans-1,2-dichloroethylene at a concentration of 200 ppm induced fatty degeneration of the hepatocytes and Kupffer cells (Freundt et al., 1977). In an additional study, exposure of rats for 8 hours to a concentration of 200 ppm cis-1,2-dichloroethylene resulted in inhibition of the MFO system as measured by hexobarbital sleeping time, zoxazolamine paralysis time and formation of 4-amino-antipyrene from aminopyrene. The cis isomer was a more potent inhibitor than the trans isomer (Freundt and Macholz, 1978). Subsequent work suggests that these effects are mediated by a P-450 generated reactive metabolite which interacts with the heme moiety at the active site of P-450 (Costa and Ivanetich, 1982). Also, it is probably nephrotoxic by analogy to 1,1-dichloroethylene (U.S. EPA, 1980a).

3.2. CHRONIC

3.2.1. Oral. Pertinent data regarding the chronic oral toxicity of cis-1,2-dichloroethylene could not be located in the available literature.

3.2.2. Inhalation. Pertinent data regarding the chronic inhalation toxicity of cis-1,2,-dichloroethylene could not be located in the available literature. In an unpublished study, Torkelsen (1965) reported no effects on growth, mortality, organ and body weights, hematology, clinical chemistry, gross pathology or histopathology in rats, rabbits, guinea pigs or dogs exposed to 500 or 1000 ppm 1,2-dichloroethylene (mixed isomers) 7 hours/day, 5 days/week for 6 months.

3.3. TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS

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

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

3.4. TOXICANT INTERACTIONS

Pertinent data regarding the interactions of cis-1,2-dichloroethylene with other toxicants could not be located in the available literature. Due to the effects of cis-1,2-dichloroethylene on cytochrome P-450, however, it would be expected that this compound could affect the toxicity of other compounds that are metabolized by the MFO system.

4. CARCINOGENICITY

4.1. HUMAN DATA

4.1.1. Oral. Pertinent data regarding the carcinogenicity of orally administered cis-1,2-dichloroethylene in humans could not be located in the available literature.

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

4.2. BIOASSAYS

4.2.1. Oral. Pertinent data regarding the carcinogenicity of orally administered cis-1,2-dichloroethylene in experimental animals could not be located in the available literature.

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

4.3. OTHER RELEVANT DATA

Greim et al. (1975) reported negative results for cis-1,2-dichloroethylene using Escherichia coli K12 as the indicator organism. Cerna and Kypenova (1977) found that cis-1,2-dichloroethylene was not mutagenic in Salmonella tester strains using the spot test without metabolic activation. cis-1,2-Dichloroethylene was found to produce a dose-dependent increase in mutations using the host-media bioassay, however, and also to induce chromosomal aberrations as indicated by cytogenic analysis of bone marrow cells isolated from mice given repeated intraperitoneal injections (Cerna and Kypenova, 1977).

cis-1,2-Dichloroethylene did not increase the recombination rate, frequency of point mutations or gene conversion in Saccharomyces cerevesiae (Galli et al., 1982).

4.4. WEIGHT OF EVIDENCE

Pertinent data regarding the carcinogenicity of cis-1,2-dichloroethylene in humans or animals could not be located in the available literature. Using the criteria for evaluating the overall weight of evidence for carcinogenicity to humans proposed by the Carcinogen Assessment Group of the U.S. EPA (Federal Register, 1984), cis-1,2-dichloroethylene is most appropriately designated a Group D-Not Classified chemical.

5. REGULATORY STANDARDS AND CRITERIA

The ACGIH (1980, 1983) has established a TLV of 200 ppm (~790 mg/m^3) and a STEL of 250 ppm (~1000 mg/m^3) based on an unpublished study by Torkelsen (1965) (see Section 3.2.2.). This standard does not distinguish between the cis and trans isomers.

6. RISK ASSESSMENT

6.1. ACCEPTABLE INTAKE SUBCHRONIC (AIS)

6.1.1. Oral. The available data were inadequate for the derivation of an oral AIS for cis-1,2-dichloroethylene.

6.1.2. Inhalation. The available data were inadequate for the derivation of an inhalation AIS for cis-1,2-dichloroethylene.

6.2. ACCEPTABLE INTAKE CHRONIC (AIC)

6.2.1. Oral. The available data were inadequate for the derivation of an oral AIC for cis-1,2-dichloroethylene.

6.2.2. Inhalation. The available data were inadequate for the derivation of an inhalation AIC for cis-1,2-dichloroethylene. The data regarding the toxicity of cis-1,2 and trans-1,2-dichloroethylene were investigated to determine the suitability for derivation of CS values based on chronic toxicity. Data were insufficient for derivation of a CS for cis-1,2-dichloroethylene.

6.3. CARCINOGENIC POTENCY (q_1^*)

6.3.1. Oral. Pertinent data regarding the carcinogenicity of cis-1,2-dichloroethylene following oral exposure could not be located in the available literature. Therefore, no q_1^* could be derived.

6.3.2. Inhalation. Pertinent data regarding the inhalation carcinogenicity of cis-1,2-dichloroethylene could not be located in the available literature. Therefore, no q_1^* could be derived.

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APPENDIX

Summary Table for cis-1,2-Dichloroethylene

	Species	Experimental Dose/Exposure	Effect	Acceptable Intake (AIS or AIC)	Reference
Inhalation					
AIS	ND	ND	ND	ND	ND
AIC	ND	ND	ND	ND	ND
Oral					
AIS	ND	ND	ND	ND	ND
AIC	ND	ND	ND	ND	ND

ND = Not derived