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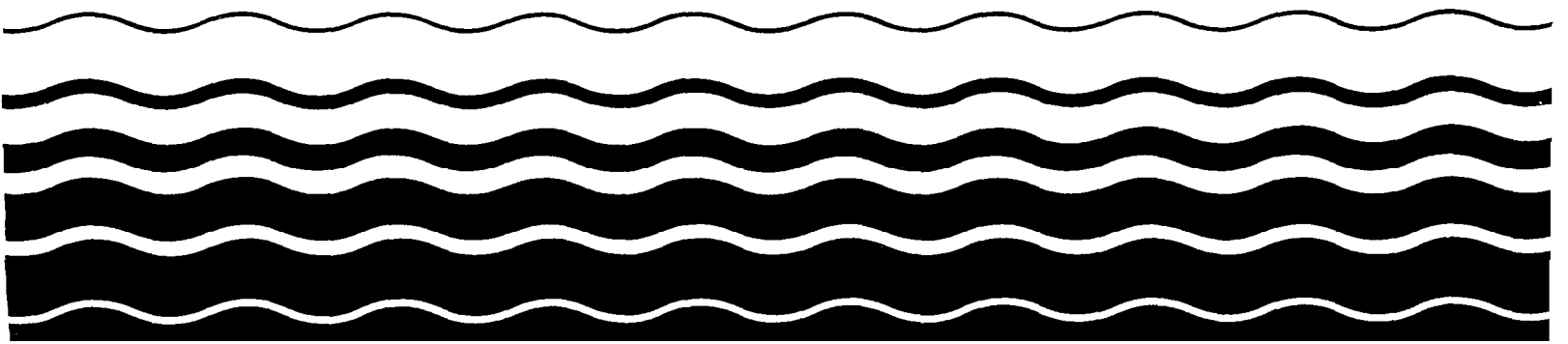
Ambient Water Quality Criteria for Dichloroethylenes



AMBIENT WATER QUALITY CRITERIA FOR

DICHLOROETHYLENES

Prepared By
U.S. ENVIRONMENTAL PROTECTION AGENCY

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FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

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ACKNOWLEDGEMENTS

Aquatic Life Toxicology

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TABLE OF CONTENTS

	Page
Introduction	A-1
Aquatic Life Toxicology	B-1
Introduction	B-1
Effects	B-1
Acute Toxicity	B-1
Chronic Toxicity	B-2
Plant Effects	B-3
Miscellaneous	B-3
Summary	B-3
Criteria	B-4
References	B-9
Mammalian Toxicity and Human Health Effects	C-1
Exposure	C-1
Ingestion from Water	C-1
Ingestion from Food	C-1
Dermal	C-3
Pharmacokinetics	C-3
Absorption	C-3
Distribution	C-4
Metabolism	C-4
Excretion	C-12
Effects	C-12
Acute, Subacute and Chronic Toxicity	C-12
Synergism and/or Antagonism	C-16
Teratogenicity	C-17
Mutagenicity	C-18
Carcinogenicity	C-19
Criterion Formulation	C-25
Existing Guidelines and Standards	C-25
Basis and Derivation of Criterion	C-26
References	C-30
Appendix	C-39

CRITERIA DOCUMENT

DICHLOROETHYLENES

CRITERIA

Aquatic Life

The available data for dichloroethylenes indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 11,600 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of dichloroethylenes to sensitive freshwater aquatic life.

The available data for dichloroethylenes indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 224,000 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of dichloroethylenes to sensitive saltwater aquatic life.

Human Health

1,1-Dichloroethylene

For the maximum protection of human health from the potential carcinogenic effects due to exposure of 1,1-dichloroethylene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentrations should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding recommended criteria are 0.33 µg/l, 0.033 µg/l, and 0.003 µg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 18.5 µg/l, 1.85 µg/l, and 0.185 µg/l, respectively.

roethylene

1,2-Dichlo

using the present guidelines, a satisfactory criterion cannot be derived

cime due to the insufficiency in the available data for 1,2-di-

at nylene.

INTRODUCTION

The dichloroethylenes consist of three isomers: 1,1-dichloroethylene (1,1-DCE), cis-1,2-dichloroethylene (cis-1,2-DCE) and trans-1,2-dichloroethylene (trans-1,2-DCE). As of the early 1960's, neither of the 1,2-dichloroethylenes (1,2-DCEs) had wide industrial usage (Patty, 1963). However, annual production of 1,1-DCE now approximates 120,000 metric tons (Arthur D. Little, Inc., 1976). It is used as a chemical intermediate in the synthesis of methylchloroform and in the production of polyvinylidene chloride copolymers (PVDCs). Among other monomers used with 1,1-DCE in copolymer production are vinyl chloride, acrylonitrile, and alkyl acrylates. The impermeability of PVDCs make them useful primarily as barrier coatings in the packaging industry. Polymers with high vinylidene chloride (1,1-DCE) content such as Saran are widely used in the food packaging industry. The heat-seal characteristics of saran coatings make them useful in the manufacture of non-flammable synthetic fiber. 1,1-DCE polymers have also been used extensively as interior coatings for ship tanks, railroad cars, and fuel storage tanks, and for coating of steel pipes and structures (Wessling and Edwards, 1970).

Dichloroethylenes are clear colorless liquids with the molecular formula $C_2H_2Cl_2$ and a molecular weight of 96.96. 1,1-DCE has a water solubility of 2,500 µg/ml, a vapor pressure of 591 mm Hg, and a melting point of -122.1°C. The cis isomer of 1,2-dichloroethylene has a water solubility of 3,500 µg/ml, a vapor pressure of 208 mm Hg, and a melting point of -80.5°C; trans 1,2-dichloroethylene has a water solubility of 6,300 /g/ml, a vapor presssure of 324 mm Hg and a melting point of -50°C (Patty, 1963; Wessling

and Edwards, 1970). The octanol/water partition coefficient for 1,1,-DCE was reported as 5.37 (log P = 0.73) by Radding, et al. (1977), indicating it should not accumulate significantly in animals.

1,1-DCE is not known to occur in nature and ambient levels have not been determined. This chemical is expected to be short-lived in water because of its volatilization to the atmosphere (Hushon and Kornreich, 1976). The 1,2-DCEs have been measured in a limited number of U.S. drinking water supplies (U.S. EPA, 1978). The population most exposed to 1,1-DCE consists of workers in industries manufacturing or using 1,1-DCE (Hushon and Kornreich, 1976; Arthur D. Little, Inc., 1976). 1,1-DCE was identified as a cocontaminant with vinyl chloride monomer in the working environment of polyvinylchloride productions plants (Kramer and Mutchler, 1972).

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U.S. EPA. 1978. Statement of basis and purpose for an amendment to the national interim primary drinking water regulations on a treatment technique for synthetic organics. Off. Drinking Water Criteria Stand. Div., U.S. Environ. Prot. Agency, Washington, D.C.

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Aquatic Life Toxicology*

INTRODUCTION

All of the available data for dichloroethylenes with one exception are for 1,1-dichloroethylene. The bluegill has been tested (U.S. EPA, 1978) with both 1,1-dichloroethylene and 1,2-dichloroethylene under similar conditions, and the 96-hour LC_{50} values under static conditions were 73,900 and 135,000 µg/l, respectively. Apparently, the location of the chlorine atoms on the molecule does not affect the acute toxicity of dichloroethylenes very much.

All of the data on the effects of dichloroethylenes on saltwater organisms are for 1,1-dichloroethylene.

EFFECTS

Acute Toxicity

Two 48-hour tests were conducted with Daphnia magna with 1,1-dichloroethylene and the EC_{50} values were 11,600 µg/l (Dill, et al. manuscript) and 79,000 µg/l (U.S. EPA, 1978) (Table 1). The cause of this difference could not be ascertained.

Dill, et al. (manuscript) tested the fathead minnow and they observed that the 96-hour LC_{50} was 169,000 µg/l using static techniques and 108,000 µg/l using flow-through techniques with measured concentrations. The value from the static test gave a lower estimate of toxicity than the flow-through test. The only additional data are for the bluegill, which was discussed

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are calculations for deriving various measures of toxicity as described in the Guidelines.

above; this species is about as sensitive to 1,1-dichloroethylene as is the fathead minnow.

The data on acute static tests with bluegill under similar conditions (U.S. EPA, 1978) in this and other documents on structurally related chemicals show a correlation between degree of chlorination and toxicity. The 96-hour LC_{50} values for this species are 73,900 and 135,000 µg/l for 1,1- and 1,2-dichloroethylene, respectively, 44,700 µg/l for trichloroethylene, and 12,900 µg/l for tetrachloroethylene. These results indicate increase in the lethal effect on bluegills with an increase in chlorine content. The correlation with Daphnia magna toxicity is not as clear. The 48-hour values from the same investigator (U.S. EPA, 1978) are 79,000, 85,200, and 17,700 µg/l for 1,1-dichloroethylene, trichloroethylene, and tetrachloroethylene, respectively.

The 96-hour LC_{50} for the mysid shrimp and 1,1-dichloroethylene is 224,000 µg/l (Table 1). The 96-hour LC_{50} for the same species under similar test conditions (U.S. EPA, 1978) is 10,200 µg/l for tetrachloroethylene. As was suggested in the freshwater part of this document, acute toxicity of these structurally related compounds increases with increasing degree of chlorination. The 96-hour LC_{50} values (Table 1) for the sheepshead minnow (U.S. EPA, 1978) and the tidewater silversides (Dawson, et al. 1977) are 249,000 and 250,000 µg/l, respectively.

Chronic Toxicity

An embryo-larval test has been conducted (U.S. EPA, 1978) with the fathead minnow and 1,1-dichloroethylene (Table 2). The range of experimental concentrations was such that no adverse effects were observed at the highest test concentration of 2,800 µg/l. The flow-through 96-hour LC_{50} for this species was 108,000 µg/l (Dill, et al. manuscript), suggesting that the dif-

ference in concentration between acute and chronic effects for the fathead minnow is less than 40 times.

No other chronic tests have been conducted on other freshwater or any saltwater species.

Plant Effects

The 96-hour EC_{50} values (Table 3), based on chlorophyll a and cell numbers of the freshwater alga, Selenastrum capricornutum, were greater than 798,000 µg/l (U.S. EPA, 1978).

There was no effect of 1,1-dichloroethylene on the saltwater alga, Skeletonema costatum, at test concentrations as high as 712,000 µg/l (Table 3).

Miscellaneous

Dill, et al. (manuscript) extended their testing with the fathead minnow and observed a 13-day LC_{50} of 29,000 µg/l for 1,1-dichloroethylene (Table 4). Their related 96-hour LC_{50} value (Table 1) was 108,000 µg/l which indicates that significant additional mortality occurred between 96 hours and 13 days.

Summary

Most of the data for dichloroethylenes and freshwater organisms are for 1,1-dichloroethylene and Daphnia magna, the fathead minnow, and the bluegill, with 50 percent effect concentrations that range from 11,600 to 169,000 µg/l. The toxicity of 1,1- and 1,2-dichloroethylene to the bluegill was similar. No chronic effects were observed for the fathead minnow at concentrations of 1,1-dichloroethylene as high as 2,800 µg/l. The tested freshwater alga was relatively insensitive to 1,1-dichloroethylene with no effects at concentrations as high as 798,000 µg/l.

All of the saltwater data are for 1,1-dichloroethylene. The range of LC_{50} and EC_{50} values for the mysid shrimp, sheepshead minnow, tidewater

silversides, and an alga is from 224,000 to greater than 712,000 µg/l. No data are available for any dichloroethylene to estimate chronic toxicity.

CRITERIA

The available data for dichloroethylenes indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 11,600 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of dichloroethylenes to sensitive freshwater aquatic life.

The available data for dichloroethylenes indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 224,000 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of dichloroethylenes to sensitive saltwater aquatic life.

Table 1. Acute values for dichloroethylenes

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Acute Value (µg/l)	Reference
		FRESHWATER SPECIES			
Cladoceran, *Daphnia magna*	S, U	1,1-dichloro-ethylene	11,600	--	Dill, et al. Manuscript
Cladoceran, *Daphnia magna*	S, U	1,1-dichloro-ethylene	79,000	30,300	U.S. EPA, 1978
Fathead minnow, *Pimephales promelas*	S, U	1,1-dichloro-ethylene	169,000	--	Dill, et al. Manuscript
Fathead minnow, *Pimephales promelas*	FT, M	1,1-dichloro-ethylene	108,000	108,000	Dill, et al. Manuscript
Bluegill, *Lepomis macrochirus*	S, U	1,1-dichloro-ethylene	73,900	73,900	U.S. EPA, 1978
Bluegill, *Lepomis macrochirus*	S, U	1,2-dichloro-ethylene	135,000	135,000	U.S. EPA, 1978
		SALTWATER SPECIES			
Mysid shrimp, *Mysidopsis bahia*	S, U	1,1-dichloro-ethylene	224,000	224,000	U.S. EPA, 1978
Sheepshead minnow, *Cyprinodon variegatus*	S, U	1,1-dichloro-ethylene	249,000	249,000	U.S. EPA, 1978
Tidewater silversides, *Menidia beryllina*	S, U	1,1-dichloro-ethylene	250,000	250,000	Dawson, et al. 1977

* S = static, FT = flow-through, U = unmeasured, M = measured

No Final Acute Values are calculable since the minimum data base requirements are not met.

Table 2. Chronic values for dichloroethylenes (U.S. EPA, 1978)

Species	Method*	Chemical	Limits (µg/l)	Chronic Value (µg/l)
	FRESHWATER SPECIES			
Fathead minnow, *Pimephales promelas*	E-L	1,1-dichloro-ethylene	>2,800	--

* E-L = embryo-larval

No acute-chronic ratio is calculable.

Table 3. Plant values for dichloroethylenes (U.S. EPA, 1978)

Species	Chemical	Effect	Result (µg/l)
	FRESHWATER SPECIES		
Alga, *Selenastrum capricornutum*	1,1-dichloroethylene	EC50 96-hr chlorophyll a	>798,000
Alga, *Selenastrum capricornutum*	1,1-dichloroethylene	EC50 96-hr cell count	>798,000
	SALTWATER SPECIES		
Alga, *Skeletonema costatum*	1,1-dichloroethylene	EC50 96-hr chlorophyll a	>712,000
Alga, *Skeletonema costatum*	1,1-dichloroethylene	EC50 96-hr cell count	>712,000

Table 4. Other data for dichloroethylenes (Dill, et al. Manuscript)

Species	Chemical	Duration	Effect	Result (µg/l)
	FRESHWATER SPECIES			
Fathead minnow, Pimephales promelas	1,1-dichloro-ethylene	13 days	LC50	29,000

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Dawson, G.W., et al. 1977. The acute toxicity of 47 industrial chemicals to fresh and saltwater fishes. Jour. Hazardous Mater. 1: 303.

Dill, D.C., et al. Toxicity of 1,1-dichloroethylene (vinylidene chloride) to aquatic organisms. Dow Chemical Company. (Manuscript)

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EXPOSURE

Ingestion from Water

The National Organic Monitoring Survey (U.S.EPA, 1978a) reported detecting, but did not quantify occurrence of one of the three dichloroethylenes (DCE) in finished drinking water, 1,1-dichloroethylene (vinylidene chloride). Fishbein (1976) indicates there is no information concerning the amount of 1,1-DCE which may migrate into water from discarded materials made from vinylidene chloride polymers. Another source of 1,1-DCE is from the decomposition of 1,1,1-trichloroethylene (McConnell, et al. 1975) which has been occasionally detected in drinking water (U.S. EPA, 1978b) usually at low concentrations (about 1.0 µg/l). The other dichloroethylenes cis-1,2-dichloroethylene (cis-1,2-DCE) and trans-1,2-dichloroethylene (trans-1,2-DCE) were found at concentrations of 16 and 1 µg/l in Miami drinking water (U.S. EPA, 1975, 1978b) Concentrations of 0.1 µg/l cis-1,2-DCE were observed in Cincinnat and Philadelphia drinking waters as well, but were absent fr seven other drinking waters included in this survey. Much t little information is available to estimate and assess curr exposure of DCE to humans via drinking water.

Ingestion from Food

Food wrappers are commonly made of 1,1-DCE copolymers. ever, there appear to be no data as to the extent to which th treated monomer migrates into foods (Fishbein, 1976). The are very volatile compounds and are degraded in air with a life of eight weeks (Pearson and McConnell, 1975).

A bioconcentration factor (BCF) relates the concentration of a chemical in aquatic animals to the concentration in the water in which they live. The steady-state BCFs for a lipid-soluble compound in the tissues of various aquatic animals seem to be proportional to the percent lipid in the tissue. Thus, the per capita ingestion of a lipid-soluble chemical can be estimated from the per capita consumption of fish and shellfish, the weighted average percent lipids of consumed fish and shellfish, and a steady-state BCF for the chemical.

Data from a recent survey on fish and shellfish consumption in the United States were analyzed by SRI International (U.S. EPA, 1980). These data were used to estimate that the per capita consumption of freshwater and estuarine fish and shellfish in the United States is 6.5 g/day (Stephan, 1980). In addition, these data were used with data on the fat content of the edible portion of the same species to estimate that the weighted average percent lipids for consumed freshwater and estuarine fish and shellfish is 3.0 percent.

No measured steady-state bioconcentration factor (BCF) is ıvailable for 1,1-dichloroethylene, but the equation "Log BCF = 0.85 Log P) - 0.70" can be used (Veith, et al. 1979) to estimate ıe steady-state BCF for aquatic organisms that contain about 7.6 rcent lipids (Veith, 1980) from the octanol/water partition coficient (P). The measured log P value was obtained from Dec, et (Manuscript). When no measured value could be found, a calcu-ɜd log P value was obtained using the method described in ch and Leo (1979). The adjustment factor of 3.0/7.6 = 0.395

is used to adjust the estimated BCF from the 7.6 percent lipids on which the equation is based to the 3.0 percent lipids that is the weighted average for consumed fish and shellfish, in order to obtain the weighted average for the edible portion of all freshwater and estuarine aquatic organisms consumed by Americans.

Chemical	Log P		Estimated Steady-State BCF	Weighted Average BCF
	Meas.	Calc.		
1,1-Dichloroethylene	2.18		14.2	5.61
1,2-Dichloroethylene (cis and trans)		1.53	4.0	1.58

Dermal

There are no data indicating the extent and significance of human exposure to dichloroethylenes via the skin.

PHARMACOKINETICS

Absorption

No animal or human studies appear to exist which specifically document the degree of systemic absorption of the DCEs by any route. However, related compounds such as trichloroethylene and tetrachloroethylene are absorbed to near the theoretical maximum for both the inhalation and ingestion routes (Daniel, 1963; Monster, et al. 1976). On this basis 35 to 50 percent of inhaled DCE and virtually 100 percent of ingested DCE may be absorbed systemically. Such a high degree of absorption of 1,1-DCE seems implied by the studies of McKenna, et al. (1977a,b) even if not specifically quantified.

Distribution

Distribution of 1,1-DCE in various organs of the rat has been studied after inhalation exposure (Jaeger, et al. 1977a) using ^{14}C-labeled 1,1-DCE. The distribution of total radioactivity 30 minutes after cessation of exposure was similar in fed and fasted rats, although the absolute level of label was considerably greater in fasted animals. The largest concentrations were found in kidney, followed by liver, spleen, heart, and brain. Blood concentrations were high relative to tissue concentrations. A similar distribution was observed for trichloroacetic acid-insoluble (TCA-insoluble), labeled material (presumably bound to macromolecules).

Subcellular distribution of radio-labeled 1,1-DCE metabolites 30 minutes following a 2-hour exposure to 8,000 mg/m^3 was observed in the microsomal, mitochondrial, and cytosolic compartments of the liver (Jaeger, et al. 1977a). However, a large amount of radioactivity in the cytosol was TCA- and $CHCl_3$-soluble, whereas that in the mitochondria and microsomes was TCA-insoluble and $CHCl_3$-soluble. These data suggest substantial binding of 1,1-DCE metabolites to macromolecules and association with the lipid present in the latter two fractions, respectively. The turnover of bound TCA-insoluble radioactivity derived from 1,1-DCE has a half-life of 2 to 3 months.

Distribution data on the 1,2-DCE isomers are not available.

Metabolism

The comparative metabolism of chloroethylenes has been extensively studied. Leibman and Ortiz (1977) have postulated th

various metabolic pathways for 1,1-DCE, cis-1,2-DCE, and trans-1,2-DCE as shown in Figure 1.

In addition, there is evidence that the 1,1-DCE metabolites are conjugated with glutathione, which presumably represents a detoxification step (McKenna, et al. 1977a). Bonse, et al. (1975) identified both the chloroethanol and chloroacetic acid derivatives of cis-1,2-DCE and trans-1,2-DCE in a perfused rat liver. The metabolism of the cis-isomer relative to the amount taken up by the liver was much greater than the trans-isomer. Leibman and Ortiz (1977) identified formation of chloroacetic acid from 1,1-DCE, but as yet the dichloroacetaldehyde has not been unequivocally identified as a metabolite of 1,1-DCE. Inhibition of epoxide hydrase resulted in a stimulation of chloroacetic acid formation from 1,1-DCE, leading to the conclusion that the glycol intermediate is relatively unimportant in the conversion of 1,1-DCE to chloroacetic acid (Leibman and Ortiz, 1977). The essential feature of each of these metabolic pathways is that all chloroethylenes appear to be metabolized through expoxide intermediates which are reactive and may form covalent bonds with tissue macromolecules (Henschler, 1977a).

In the intact animal, a large portion of the systemically absorbed 1,1-DCE is metabolically converted. Jaeger, et al. (1977a) found 36.7 + 3.3 percent of the absorbed dose in the urine of rats within 26 hours. Disposition of ^{14}C-activity from radio-labeled 1,1-DCE in mice and rats over a 48-hour period (McKenna, et al. 1977b) is shown in Table 1.

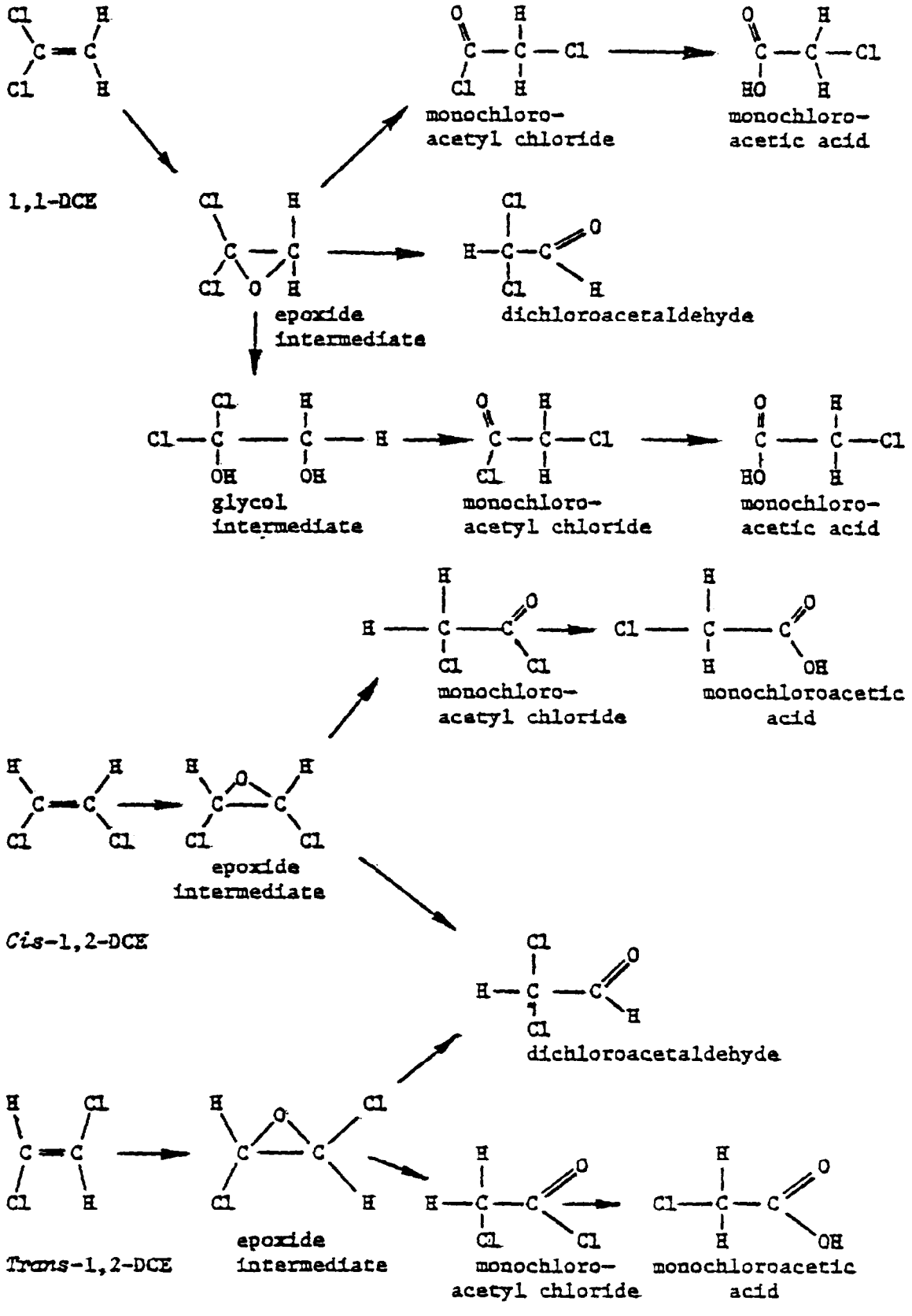

FIGURE 1

Proposed Metabolic Pathways of 1,1-DCE
and the 1,2-DCE Isomers
Source: Leibman and Ortiz, 1977

TABLE 1

Disposition of 1,1-DCE Following Inhalation of 40 mg/m^3 Over a 40-hour Period*

	Mice	Rats
Expired 1,1-DCE %	0.65 ± 0.07	1.63 ± 0.14
Expired $^{14}CO_2$	4.64 ± 0.17	8.74 ± 3.72
Body Burden %		
Urine	80.83 ± 1.68	74.72 ± 2.30
Feces	6.58 ± 0.81	9.73 ± 0.10
Carcass	5.46 ± 0.41	4.75 ± 0.78
Cage Wash.	1.83 ± 0.84	0.44 ± 0.28
Body Burden mg. eq.		
1,1-DCE/kg	5.30 ± 0.75	2.89 ± 0.24
Total Metabolized		
mg. eq. 1,1-DCE/kg	5.27 ± 0.74	2.84 ± 0.26

*Source: McKenna, et al. 1977b.

It is clear from these data that the mouse develops a higher body burden of 1,1-DCE than the rat at identical exposure levels. The disposition of 1,1,-DCE appears quite similar in the two species. However, as a result of the overall greater rate of metabolism, covalently bound 1,1-DCE metabolites are higher in the mouse than in the rat as shown in Table 2. The substantial difference in distribution may be related to the differing sensitivity of the species to carcinogenic effects of 1,1-DCE (Hathaway, 1977).

In a study where mice and rats were administered an oral dose (50 mg/kg) of 1,1-DCE, mice were found to metabolize a greater proportion of DCE (Jones and Hathaway, 1978). Although DCE was metabolized in much the same way in both species (Table 3), mice formed considerably more of the N-acetyl-S-cysteinyl acetyl derivative, and excrete a small amount of N-acetyl-S-(2-carboxymethyl)-cysteine, which was not found in the rat.

Jones and Hathaway suggested that the efficiency of DCE metabolism in rats and mice follows the activity of cytochrome P-450 in the organs of these animals, and that "real exposure" (expressed in the amount of DCE metabolized) is relatively higher for orally dosed mice than rats.

It is notable that in both species, covalently bound metabolites of 1,1-DCE are highest in kidney followed by liver. Exposure of rats by inhalation to a higher concentration (8,000 mg/m^3) for a shorter period (two hours) appears to give somewhat differing results. In this case, a high degree of TCA-insoluble ^{14}C-activity is observed in the liver. These differences

TABLE 2

Covalently Bound ^{14}C-Activity in Rat and Mouse Following Exposure to 40 mg/m^3 ^{14}C-1,1-DCE*

	^{14}C-1,1,-DCE, µg eq/mg Protein	
	Liver	Kidney
Mice	22.29 ± 3.77	79.55 ± 19.11
Rats	5.28 ± 0.14	13.14 ± 1.15

*Source: McKenna, et al. 1977b.

TABLE 3

Relative Proportion of (^{14}C) Excretory Products After Oral Administration of 50 mg/kg of (1-^{14}C)DCE to Rodents†

(^{14}C) Excretory Products	^{14}C Expressed as % of Dose	
	Mice*	Rats*
Unchanged DCE } pulmonary	6	28
CO_2 } excretion	3	3.5
Chloroacetic acid	0	1
Thiodiglycollic acid	3	22
Thioalycollic acid	5	3
Dithioglycollic acid	23	5
Thioglycollyloxalic acid	3	2
N-Acetyl-S-cysteinyl acetyl derivative	50	28
N-Acetyl-S-(2-carboxymethyl) cysteine	4	0
Urea	3	3.5

†Source: Jones and Hathaway, 1978.
*Alderly Park strains.

between long- and short-term inhalation exposures must be kept in mind when evaluating the long-term toxicity of 1,1-DCE.

The relationship of metabolism of DCEs to their toxicity is not well understood. Differing results are obtained with inducers and inhibitors of microsomal enzymes depending upon the age or body weight of experimental animals (Anderson and Jenkins, 1977). Pretreatment with dithiocarbamates, which presumably interfere with 1,1-DCE metabolism, protects against lethal and hepatotoxic damage (from 1,1-DCE) and reduces covalent binding of metabolites to tissue macromolecules (Short, et al. 1977a) On the other hand, Aroclor 1254 or phenobarbital pretreatment, which would increase microsomal enzyme activity, also decreases the hepatotoxicity of 1,1-DCE (Reynolds, et al. 1975; Jenkins, et al. 1972). However, Carlson and Fuller (1972) reported increased mortality from 1,1-DCE in rats following phenobarbital pretreatment. The possibilities that these pretreatments either intereact with more than one metabolic pathway or that differing mechanisms account for hepatotoxicity and lethality of 1,1-DCE, or both, could account for the inconsistent responses (Anderson and Jenkins, 1977; Reynolds and Moslen, 1977). It is clear that the hepatotoxicity of 1,1-DCE does increase with decreasing concentrations of hepatic glutathione (Jaeger, et al. 1973). This seems involved with the greater sensitivity of fasted animals to 1,1-DCE-induced hepatotoxicity (Jaeger, et al. 1974). In regard to this issue, Hathaway (1977) has identified thiodiglycollic acid, thioglycollic acid, dithioglycollic acid, and an N-acetyl-S-cysteinyl-acetyl derivative as products of 1,1-DCE metabolism in rats and mice.

Excretion

There appear to be no data relating to the rate at which any of the DCEs are cleared from the body. In the case of 1,1-DCE one can guess that the rate of elimination is relatively rapid in that substantial fractions of the total absorbed dose may be recovered in urine within 26 or 72 hours (Jaeger, et al. 1977a; McKenna, et al. 1977a). However, these data do not allow a more precise estimate of turnover. Disappearance of covalently bound metabolites of 1,1-DCE (measured as TCA-insoluble fractions) appears to be fairly rapid as well, with a reported half-life of 2 to 3 hours (Jaeger, et al. 1977a). These data were obtained from experiments of insufficient duration and resolution of the nature of the binding to rule out the possibility of a residual binding to tissue macromolecules of an irreversible or slowly reversible character.

No data exist concerning the excretion of the cis- or trans-isomers of 1,2-DCE.

EFFECTS

Acute, Subacute, and Chronic Toxicity

Like other members of the chlorinated ethylene series, the DCEs possess anesthetic properties. Unlike those compounds of the group which were employed as general anesthetics, very little effort has gone into characterizing either short- or long-term CNS toxicity of the DCEs. Irish (1962) referenced unpublished data concerning the CNS depressant activity of 1,1-DCE in humans. A concentration of 16,000 mg/m^3 was estimated as sufficient to rapidly produce a state resembling drunkenness and was felt likely

to result in unconsciousness if exposure was continued. A single report has been made associating sensory disturbances in the area of the face controlled by the trigeminal nerve and accidental exposure to 1,1-DCE (Broser, et al. 1970). Subsequent evaluation, however, suggested that the toxic agent was either mono- or dichloroacetylene which was a contaminant of 1,1-DCE (Henschler, et al. 1970). No further information exists concerning the central nervous system toxicity of these compounds.

In recent years, considerable attention has focused on the liver and kidney damage produced by 1,1-DCE. Prendergast, et al. (1967) documented morphological damage to kidney and liver of rats and guinea pigs exposed to 1,1,-DCE at 189 mg/m^3. These effects were associated with an increase liver lipid concentration in rats. In guinea pigs, continuous 90-day exposure to concentrations as low as 20 mg/m^3 produced increased mortality, whereas intermittent exposures (30 exposures, 8 hours/day, 5 days/week) at 395 mg/m^3 produced no increase in mortality. A similar difference in intermittent versus continuous exposures was observed in the monkey where increased mortality was observed with continuous exposure at a concentration of 101 mg/m^3. No mortality was observed with the same intermittent exposure utilized for guinea pigs.

Results of a 90-day toxicity study in rats given 1,1-DCE in water or in air revealed cytoplasmic vacuolization in liver cells of rats ingesting 200 ppm or inhaling 25 ppm of the compound. The hepatocellular changes were interpreted to be of a reversible character (Quast, et al. 1977).

Oral administration of single doses of 1,1-DCE at 200 and 400 mg/kg decreases liver glucose-6-phosphatase, increases liver alkaline phosphatase, liver tyrosine transaminase, plasma alkaline phosphatase, and plasma alanine transaminase (Jenkins, et al. 1972) 20 hours after administration. The LD_{50} of 1,1-DCE was decreased in adrenalectomized rats (1,550 mg/kg in sham-operated, 84 mg/kg in adrenalectomized animals) by a factor of 20. This effect was not clearly related to the hepatotoxicity of 1,1-DCE (Jenkins, et al. 1972).

The hepatotoxic effects of 1,1-DCE appear to be potentiated by depletion of hepatic glutathione concentrations, whether resulting from normal diurnal variation (Jaeger, et al. 1973) or by fasting (Jaeger, et al. 1974, 1975). In the latter case, it was possible to demonstrate increased concentrations of 1,1-DCE in blood and liver in the fasted animals. Thyriodectomy decreased whereas thyroxine administration exacerbated the hepatotoxic effects of 1,1-DCE (Szabo, et al. 1977; Jaeger, et al. 1977b). At the same time thyroidectomy increased, and thyroxine decreased liver glutathione concentrations. Jaeger (1977) has suggested that the hepatotoxic effects of 1,1-DCE are secondary to a reduction in mitochondrial glutathione (and sulfhydryl enzymes) and marked inhibition of mitochondrial respiration.

Jenkins, et al (1972) found both cis- and trans-1,2-DCE to be considerably less potent than 1,1-DCE as a hepatotoxin. Freundt, et al. (1977) indicated that repeated inhalation exposures of 800 mg/m^3 (8 hours/day, 5 days/week, 16 weeks) of the trans-1,2-DCE produces fatty degeneration of the liver.

Less attention has been paid to the renal toxicity of the DCEs despite the occurence of histologically demonstrated damage at 1,1-DCE exposures equal to or less than those required for hepatotoxicity (Prendergast, et al. 1967; Short, et al. 1977a). The degree of covalent binding of 1,1-DCE metabolites has been shown to be higher in kidney than in liver in both rats and mice (McKenna, et al. 1977b; Short, et al. 1977a) suggesting that renal damage resulting from 1,1-DCE should be more carefully examined in the future. No quantitative data appear available on the nephrotoxicity of 1,2-DCEs. Inhalation of 1,1-DCE at high concentrations (102,000 mg/m^3) for short periods of time (10 minutes) has been found to sensitize the myocardium to arrhythmias produced by injection of epinephrine (Siletchnik and Carlson, 1974). Unlike hepatotoxicity, the cardiac sensitizing effects of 1,1-DCE were enhanced by phenobarbital pretreatment. This implies that a metabolite of 1,1-DCE may be involved. Similar effects have been observed in human poisoning with trichloroethylene. The 1,2-DCE isomers have not been investigated with respect to this effect.

Only one epidemiological study has been published which examined workers exposed to 1,1-DCE uncomplicated by exposures to other solvents (Ott, et al. 1976). At the time of this preliminary report, no abnormal findings could be associated with 1,1-DCE exposure in a population of 138 workers. Measured concentrations in the workplaces of these individuals ranged from 9 to 280 mg/m^3 (time-weighted averages).

As reported with a number of other chlorinated hydrocarbon solvents, 1,1,-DCE increases bile-duct pancreatic fluid flow in

fasted rats (Hamada and Peterson, 1977). The composition of the fluid did not differ significantly from that in control animals. The significance of this finding remains to be established.

Synergism and/or Antagonism

DCEs are metabolically converted to reactive epoxide intermediates (Bonse, et al, 1975; Hathaway, 1977; McKenna, et al. 1977b). Consequently, it would be predicted that compounds which increase or decrease the rate of DCE metabolism would affect toxicity. However, interactions at this level do not at present lend themselves to simple prediction. Compounds which decrease covalent binding of 1,1-DCE metabolites, such as disulfiram, protect against lethality and hepatotoxicity resulting from 1,1-DCE exposure (Short, et al. 1977a). On the other hand, pretreatment of animals with inducers of microsomal enzyme systems, such as Aroclor 1254 or phenobarbital, appear to decrease the hepatotoxicity due to 1,1-DCE (Reynolds, et al. 1975; Jenkins, et al. 1972), but increase mortality (Carlson and Fuller, 1972). These conflicting findings suggest that metabolism of the DCEs is not sufficiently understood to allow straightforward predictions. It is likely that the degree of conjugation of reactive intermediates with glutathione may be the factor not yet taken into account in attempting to predict the impact of altering microsomal enzyme activities on toxicity (Hathaway, 1977).

Although tissue glutathione concentrations affect the hepatotoxicity of 1,1-DCE (Jaeger, et al. 1973, 1977b), decreased tissue

glutathione is associated with greater toxicity and elevated glutathione with decreased toxicity in response to 1,1-DCE challenge.

Thyroidectomy decreases and adrenalectomy greatly potentiates the toxicity of 1,1-DCE (Szabo, et al. 1977; Jenkins, et al. 1972), by altering glutathione levels.

Teratogenicity

Murray, et al. (1979) evaluated the teratogenic potential of inhaled or ingested 1,1-DCE in Sprague-Dawley rats and New Zealand white rabbits. Inhalation exposure for both species was for 7 hours/day at 20 (rats only), 80, and 160 ppm. In the ingestion study, rats were given drinking water with 200 ppm DCE, or approximately 40 mg/kg/day. Administration for rats was on days 6 to 15 of gestation, and for rabbits, the 6th to 18th day. In rats, inhalation of 80 to 160 ppm of DCE produced significant maternal effects including decreased weight gain, decreased food consumption, increased water consumption, and increased liver weight (160 ppm only). In the offspring, there was a significantly increased incidence of skeletal alterations at 80 and 160 ppm; these alterations included wavy ribs and delayed ossification of various bones. In rabbits, 160 ppm caused a significant increase in resorptions in the dams, and in the offspring, a significant change in several minor skeletal variations. In both rats and rabbits exposed to 1,1-DCE by inhalation, Murray, et al. (1979) noted that concentrations which caused little evidence of maternal toxicity (20 ppm in the rat and 80 ppm in the rabbit) caused no adverse effect on embryonal or fetal development.

In rats receiving DCE by ingestion, the only significant effect noted was an increase in mean fetal crown rump length (Murray, et al. 1979).

Mutagenicity

1,1-DCE has been shown to be mutagenic in Salmonella typhimurium strains TA1530 and TA100 (Bartsch, et al. 1975) and E. coli K12 (Greim, et al. 1975). In both systems mutagenic activity required microsomal activation. Pretreatment with phenobarbital increased the mutagenic activity produced by microsomal fractions derived from liver, kidney, or lung (Bartsch, et al. 1975). Microsomal preparations, particularly liver, were considerably more active when derived from mice than from rats (Bartsch, et al. 1975).

Both the cis- and trans-isomers of 1,2-DCE were nonmutagenic when assayed with E. coli K12 at similar concentrations used for 1,1-DCE (Greim, et al. 1975). Henschler (1977a) and his associates have suggested that the mutagenic and presumably carcinogenic activities of the chloroethylene series are related to the unsymmetrical chlorine substitution or the respective epoxide intermediates. Such substitution would result in less stable and more reactive intermediates than symmetricaly substituted epoxides. These data support this hypothesis, at least with respect to mutagenesis in the E. coli K12 system. However, generalization of this hypothesis to carcinogenesis in intact animals is not yet possible and requires modification to account for the demonstrated carcinogenic activity of tetrachloroethylene [National Cancer Institute (NCI), 1977]. In addition, both 1,1,-DCE and cis-1,2-DCE

were found mutagenic in Salmonella tester strains (Cerna and Kypenova, 1977). The trans-1,2-DCE isomer was found inactive. Of the three DCEs, only cis-1,2-DCE promoted chromosomal aberrations in cytogenic analysis of bone marrow cells with repeated i.p. injections (Cerna and Kypenova, 1977).

The finding of increased mutation rates in bacterial systems has not been confirmed in mammalian systems. Adult CD male rats exposed to 220 mg 1,1-DCE/m^3 for 6 hours/day, 5 days/week for 11 weeks failed to produce dominant lethal mutations (Short, et al. 1977b). Similar results have been reported by Anderson, et al. (1977) in dominant lethal studies in CD-1 mice.

Carcinogenicity

The carcinogenicity of 1,1-DCE is currently being evaluated in studies sponsored by the National Cancer Institute (1978). No results are yet available. Maltoni, et al. (1977) and Maltoni (1977) have reported preliminary results with inhalation exposures to 1,1-DCE. Exposure conditions were 4 hours/day, 4 to 5 days/week for 52 weeks to 100 mg 1,1-DCE/m^3. Animals at the time of the report had been observed for a total of 98 weeks. At this concentration 17 of these mice had developed kidney adenocarcinomas. No kidney adenocarcinomas had been observed in the control animals. The majority of tumors were observed in male mice as shown in Table 4. In this same study, no kidney adenocarcinomas were observed in Sprague-Dawley rats at exposure up to 800 mg/m^3 1,1,-DCE.

TABLE 4

Kidney Adenocarcinomas in Swiss Mice Exposed to 100 mg/m^3 1,1-DCE Starting at 9 Weeks of Age*

1,1-DCE	Sex	Total Animals at Risk**	No. Animals with Adenocarcinoma	%
None	Male	54	0	0
None	Female	49	0	0
100 mg/m^3	Male	78	16	20.5
100 mg/m^3	Female	65	1	1.5

*Source: Maltoni, et al. 1977.

**Defined here as the number of animals that had died since the appearance of the first tumor; or (survivors at the time of the first tumor) - (survivors at the time these preliminary data were reported).

Maltoni, et al (1977) also observed a significant increase in mammary adenocarcinomas in Swiss mice inhaling 100 mg 1,1-DCE/m^3 and Sprague-Dawley rats exposed to 600 mg/m^3 under the same conditions. The mouse data are presented in Table 5 and the rat data in Table 6. Experiments in female Sprague-Dawley rats exposed to 20 mg 1,1-DCE by gavage 4 to 5 days/week for 52 weeks resulted in a 42 percent incidence of mammary tumors, whereas control animals had a 34 percent incidence. These latter data were not analyzed statistically. Finally, these authors also found that hamsters exposed to the same conditions as the Swiss mice failed to exhibit an increased tumor incidence.

In another study, Lee, et al. (1977) observed a small increase in hepatic hemangiosarcomas in mice exposed to 220 mg/m^3 1,1-DCE, 6 hours/day, 5 days/week for 7 to 12 months. Although kidney pathology was observed, no mention was made of kidney adenocarcinomas.

Rampy, et al. (1977) exposed male and female Sprague-Dawley rats to 200 mg 1,1-DCE/l in drinking water (two years) or 100 and 300 mg/m^3 1,1-DCE by inhalation (6 hours/day, 5 days/week for 18 months). In their interim report, there was no evidence (based on total tumor count) of increased tumor incidence in animals treated with 1,1-DCE. An unpublished final report of the Rampy study by Humiston, et al. (1977) agreed with the interim conclusion.

The only human data concerning possible carcinogenic effects of 1,1,-DCE in man appeared in the epidemiological study of approximately 30 employees by Ott, et al. (1976). No associations

TABLE 5

Incidence of Mammary Adenocarcinomas in Female Swiss Mice Receiving 1,1-DCE via Inhalation†

	0 mg/m^3	40 mg/m^3	0 mg/m^3	100 mg/m^3
Age at start of test (weeks)	16	16	9	9
Number with tumors/number at risk*	2/52	1/20	0/49	7/65
Incidence	3.8	5.0	0	10.8
p-values**	----	0.63	----	0.017

†Source: Maltoni, et al. 1977.

*Number of risk defined here as the number of animals that had died since the appearance of the first tumor (a kidney adenocarcinoma); or (survivors at time of the first tumor) - (survivors at the time these preliminary data were reported).

**Calculated using Fisher exact test and matched control incidence.

TABLE 6

Incidence of Mammary Tumors in Rats Inhaling 1,1-DCE*

Number with tumors	0	40	100	200	400	600
Number initially	32/100	15/30	12/30	15/30	18/30	35/60
Incidence	0.32	0.05	0.40	0.50	0.60	0.58
P-Values**		0.058	0.27	0.058	0.0058	0.001

*Source: Maltoni, et al. 1977.

**Calculated using the Fisher exact test.

could be made between cancer deaths and exposure to 1,1-DCE. The population was too small to evaluate the carcinogenicity of 1,1-DCE.

CRITERION FORMULATION

Existing Guidelines and Standards

Standards that have been established for the DCEs are applicable primarily to occupational exposures. The threshold limit values (TLV) for these compounds presently established by the American Conference of Governmental Industrial Hygienists (ACGIH) are 40 mg/m^3 (1,1-DCE) and 790 mg/m^3 (1,2-DCE). These values allow daily exposures of 286 mg 1,1-DCE and 5,643 mg 1,2-DCE. These calculations are based on the assumption of a 50 m^3/work week of inhaled air averaged over a 7-day period (Stokinger and Woodward, 1958). A separate standard has been established for 1,1-DCE, but the TLV does not distinguish between the two isomers of 1,2-DCE.

The standard for 1,2-DCE was established on the basis of no measurable effects on growth, mortality, organ and body weights, hematology, clinical chemistry, and gross and microscopic pathology at doses of up to 4,000 mg/m^3 for six months in rats, rabbits, guinea pigs and dogs (ACGIH, 1977). However, more recent data (Freundt, et al. 1977) indicate that 16 weeks of exposure at the TLV of 790 mg/m^3 of trans-1,2-DCE produces histological evidence of fatty degeneration of the liver in rats.

In the case of 1,1-DCE, the standard was established primarily on the basis of the work of Prendergast, et al. (1967) who observed increased mortality as a result of continuous 90-day exposures of 1,1-dichloroethylene to guinea pigs at 20 mg/m^3 or to monkeys at 101 mg/m^3. Liver and kidney pathology were observed at 189 mg/m^3 in rats and guinea pigs. As can be seen

these industrial TLVs allow very little safety factor for sensitive populations. Moreover, recent data suggesting that 1,1-DCE is carcinogenic in mice (Maltoni, 1977) have not yet been taken into account.

Basis and Derivation of Criterion

The use of TLV data assumes an 8-hour day, time-weighted average, occupational exposure in the work place with workers inhaling the toxic substance throughout such period. Exposures for the general population should be considerably less. Such worker-exposure inhalation standards are inappropriate for the general population since they presume an exposure limited to an 8-hour day, an age bracket of the population that excludes the very young and the very old, and a healthy worker prior to exposure. Ingestion data are far superior to inhalation data when the risks associated with the food and water environment are being considered. Recent data suggest that the ACGIH estimate of noncarcinogenic risks resulting from exposure to the DCEs may approximate effect levels for 1,1-DCE. Additionally, it is recognized that the ACGIH standards apply primarily to healthy adult worker populations and do not incorporate safety factors for sensitive populations. In order to provide a wider margin of safety, calculations of acceptable concentrations of DCEs in drinking water as proposed by Stokinger and Woodward (1958) include a safety factor of 100 and are illustrated as follows:

1,1-DCE $$\frac{40\ mg/m^3 \times 50\ m^3/week \times 0.40^*}{7\ days/week \times 100^{**}} = 1.14\ mg/day$$

* Estimated coefficient of absorption via inhalation vs. ingestion.
**Safety factor for sensitive populations.

The safety factor of 100 was based upon the rationale of the National Academy of Sciences (NAS) for noncarcinogenic substances where limited human data and valid animal studies exist (NAS, 1977). The absorption coefficient is based on the data of Monster, et al. (1976) for the related compound, trichloroethylene. Assuming a 2 liter daily consumption of drinking water, concentrations of 1,1-DCE should be limited to 0.6 mg/l (1.14 mg/day/2 liters) on the basis of noncarcinogenic risks.

However, under the Consent Decree in NRDC v. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." 1,1-Dichloroethylene is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of 1,1-dichloroethylene in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of 1,1-dichloroethylene corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the Federal Register notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria for 1,1-dichloroethylene at an interim target risk level of 10^{-5}, 10^{-6}, or 10^{-7} as shown in the following table.

Exposure Assumtpions (per day)	Risk Levels and Corresponding Criteria (1)		
	10^{-7}	10^{-6}	10^{-5}
2 liters of drinking water and consumption of 6.5 g fish and shellfish. (2)	0.003 µg/l	0.033 µg/l	0.33 µg/l
Consumption of fish and shellfish only.	0.185 µg/l	1.85 µg/l	18.5 µg/l

(1) Calculated by applying a linearized multistage model, as described in the Human Health Methodology Appendices to the October 1980 Federal Register notice which announced the availability of this document, to the animal bioassay data presented in the Appendix and in Table 4. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

(2) Approximately 2 percent of the 1,1-dichloroethylene exposure results from the consumption of aquatic organisms

which exhibit an average bioconcentration potential of 5.61-fold. The remaining 98 percent of 1,1-dichloroethylene exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of 1,1-dichloroethylene (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding 1,1-dichloroethylene concentrations and (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding 1,1-dichloroethylene concentrations. Because data indicating other sources of 1,1-dichloroethylene exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

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APPENDIX

Derivation of Criterion for 1,1-Dichloroethylene

Maltoni (1977) exposed Swiss mice via inhalation to 25 ppm (group IV in his Table 7) of 1,1,-dichloroethylene for 4 hrs/day, 4.5 days/week for 52 weeks. The interim report summarized the results after 82 weeks. The number of males alive at the time of the first kidney adenocarcinoma (55 weeks) were 98 and 70 in the treated and control (group VII) groups, respectively. At 82 weeks 20 and 16 animals were alive in treated and control groups, respectively, and the remaining animals were examined histologically. The results were that 16 of treated males had kidney adenocarcinomas, whereas none of the control animals had these tumors.

The average dose in mg/kg/day is calculated from the concentration (25 ppm) and the breathing rate (assumed to be a standard rate of 0.0375 m^3/day for 30 gm mice) as follows, where 1 ppm of dichloroethylene is assumed to be equivalent to 4 mg/m^3 in air:

The lifetime average dose is:

$$25 \text{ ppm} \times (4/24) \times (4.5/7) \times (52/82) = 1.699 \text{ ppm}$$

Converting to mg/kg/day:

$$D = 1.699 \text{ ppm} \times (4 \text{ mg/m}^3 \text{ per ppm}) \times (0.0375 \text{ m}^3 \text{ of air/day} \times (1/0.03 \text{ kg}) = 8.502 \text{ mg/kg/day}.$$

The parameters of the risk extrapolation are:

Dose mg/kg/day)[a]	Incidence (no. responding/no. tested)
0.0	0/54
8.5	16/78

le = 52 weeks w = 0.030 kg

Le = 82 weeks R = 5.61 l/kg

L = 90 weeks

With these parameters the carcinogenic potency factor for humans, q_1^*, is 1.04 $(mg/kg/day)^{-1}$. This leads to the estimate that the water concentration should be less than 0.33 µg/l in order to keep the lifetime risk to 1,1-dichloroethylene less than 10^{-5}.

[a]This value of dose has already been adjusted for the length of the experiment (i.e., it has been multiplied by le/Le).

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