CHLORINATED ETHANES

Ambient Water Quality Criteria

Criteria and Standards Division
Office of Water Planning and Standards
U.S. Environmental Protection Agency
Washington, D.C.

CRITERION DOCUMENT

CHLORINATED ETHANES

CRITERIA

Aquatic Life

1,2-dichloroethane

The data base for freshwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For 1,2-dichloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 3,900 µg/l as a 24-hour average and the concentration should not exceed 8,800 µg/l at any time.

The data base for saltwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For 1,2-dichloroethane the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 880 µg/l as a 24-hour average and the concentration should not exceed 2,000 µg/l at any time.

1,1,1-trichloroethane

The data base for freshwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For 1,1,1-trichloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 5,300 µg/l as a 24-hour average and the concentration should not exceed 12,000 µg/l at any time.

The data base for saltwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For 1,1,1-trichloroethane the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 240 µg/l as a 24-hour average and the concentration should not exceed 540 µg/l at any time.

1,1,2-trichloroethane

The data base for freshwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For 1,1,2-t ichloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 310 µg/l as a 24-hour average and the concentration should not exceed 710 µg/l at any time.

For saltwater aquatic life, no criterion for 1,1,2-trichloroethane can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

1,1,1,2-tetrachloroethane

The data base for freshwater aquatic life is insufficient to allow use of the Guidelines. The following recommenda-

tion is inferred from toxicity data on pentachloroethane and saltwater organisms.

For 1,1,1,2-tetrachloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 420 µg/l as a 24-hour average and the concentration should not exceed 960 µg/l at any time.

For saltwater aquatic life, no criterion for 1,1,1,2-tetrachloroethane can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

1,1,2,2-tetrachloroethane

The data base for freshwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For 1,1,2,2-tetrachloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 170 µg/l as a 24-hour average and the concentration should not exceed 380 µg/l at any time.

The data base for saltwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For 1,1,2,2-tetrachloroethane the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 70 µg/l as a 24-hour average and the concentration should not exceed 160 µg/l at any time.

Pentachloroethane

The data base for freshwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For pentachloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 440 µg/l as a 24-hour average and the concentration should not exceed 1,000 µg/l at any time.

For pentachloroethane the criterion to protect saltwater aquatic life as derived using the Guidelines is 38 µg/l as a 24-hour average and the concentration should not exceed 87 µg/l at any time.

Hexachloroethane

The data base for freshwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For hexachloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 62 µg/l as a 24-hour average and the concentration should not exceed 140 µg/l at any time.

The data base for saltwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data on pentachloroethane and saltwater organisms.

For hexachloroethane the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 7.0 µg/l as a 24-hour average and the concentration should not exceed 16 µg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to 1,2-dichloroethane, 1,1,2-trichloroethane, 1,1,2,2-tetrachloroethane and hexachloroethane through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of these chlorinated ethanes estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria as follows:

Compound	Risk Levels and Corresponding Criteria		
	10^{-5}	10^{-6}	10^{-7}
1,2-dichloroethane	7.0 µg/l	.70 µg/l	.07 µg/l
1,1,2-trichloroethane	2.7 µg/l	.27 µg/l	.027 µg/l
1,1,2,2-tetrachloroethane	1.8 µg/l	.18 µg/l	.018 µg/l
hexachloroethane	5.9 µg/l	.59 µg/l	.059 µg/l

For the protection of human health from the toxic properties of 1,1,1-trichloroethane ingested through the consumption of water and fish, the criterion is 15.7 mg/l.

At the present, there are insufficient data to derive criteria for monochloroethane, 1,1-dichloroethane, 1,1,1,2-tetrachloroethane and pentachloroethane.

CHLORINATED ETHANES

Introduction

The chlorinated ethanes are produced in large quantities and used for production of tetraethyl lead and vinyl chloride as industrial solvents, and as intermediates in the production of other organochlorine compounds. All of the chlorinated ethanes studies are at least mildly toxic, toxicity increasing with degree of chlorination. Some have been found in drinking waters, in natural waters, and in aquatic organisms and foodstuffs.

There are nine chlorinated ethanes, the properties of which vary with the number and position of the chlorine atoms (see Table 1). Both water solubility, in most cases, and vapor pressure decrease with increasing chlorination, while density and melting point increase. Chloroethane is a gas at room temperature; hexachloroethane is a solid; the rest are liquids. All are sufficiently soluble to be of potential concern as water pollutants. The only member of the series with a specific gravity less than 1 is chloroethane (S.G. O. 9214).

The chlorinated ethanes form azeotropes with water (Kirk and Othmer, 1963), a characteristic which could influence their persistences in the water column. All are very soluble in organic solvents (Lange, 1956). The chlorinated ethanes undergo the usual dehalogenation and dehydrohalogenation reactions of chlorinated aliphatic ompounds in the laboratory (Morrison and Boyd, 1966).

Pearson and McConnell (1975) were unable to demonstrate microbial degradation of the chlorinated ethanes, but did report chemical degradation of chlorinated hydrocarbons.

Chlorinated ethanes do not bioconcentrate significantly; however, they do exhibit a greater bioconcentrating potential with increased chlorination. Bluegill are found to bioconcentrate hexachloroethane at a factor of nearly 140, whereas they bioconcentrate dichloroethane at 2.

Acute toxicity to both freshwater and marine vertebrates and invertebrates seems to be dependent on the number of chlorine atoms associated with the ethane molecule. Pentachloroethane, in several instances, is the exception to this observation (e.g., freshwater invertebrates and saltwater fishes). Aquatic chronic toxicity data are sparce.

In regard to human and mammalian health, no literature concerning the teratogenicity of the chlorinated ethanes was found. Mutagenicity data were non-existent except for a finding that showed the mild mutagenesis of 1,2-di- and 1,1,2,2-tetrachloroethane in the Ames Salmonella assay. 1,2-Dichloroethane induced a higher frequency of somatic mutations in Drosophila. 1,2-Di-; 1,1,2-tri-; 1,1,2,2-terta-; and hexachloroethanes have all proved to be carcinogenic in rodents.

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AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Acute toxicity determinations on compounds of this class have been conducted with bluegill, Daphnia magna, and Selenastrum capricornutum. No chronic effects data are available.

Acute Toxicity

All data reported for bluegill are from 96-hour static toxicity tests with measured concentrations (Table 1). The unadjusted 96-hour LC50 values for 1,2-dichloroethane were 550,000 µg/l (Dawson, et al. 1977) and 431,000 µg/l (U.S. EPA, 1978). The other unadjusted bluegill 96-hour LC50 values (U.S. EPA, 1978) were: 1,1,1-trichloroethane - 69,700 µg/l, 1,1,2-trichloroethane - 40,200 µg/l, 1,1,1,2-tetrachloroethane - 19,600 µg/l, 1,1,2,2-tetrachloroethane - 21,300 µg/l, pentachloroethane - 7,240 µg/l, and hexachloroethane - 980 µg/l.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] 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 the calculations for deriving various measures of toxicity as described in the Guidelines.

Alexander, et al. (1978) conducted acute toxicity tests with the fathead minnow and 1,1,1-trichloroethane under static and flow-through conditions with unmeasured and measured concentrations, respectively (Table 1). The flow-through, measured LC50 value before adjustment (52,800 µg/l) is about one-half that (105,000 µg/l) for the static, unmeasured LC50 value. After adjustment the values are essentially the same and this result indicates that the adjustment values for test conditions are probably appropriate for 1,1,1-trichloroethane.

Unadjusted 48-hour LC50 values for Daphnia magna are (Table 2): 1,2-dichloroethane - 218,000 µg/l, 1,1,2-trichloroethane - 18,000 µg/l, 1,1,1,2-tetrachloroethane - 23,900 µg/l, 1,1,2,2-tetrachloroethane - 9,320 µg/l, pentachloroethane - 62,900 µg/l, and hexachloroethane - 8,070 µg/l. The 48-hour LC50 value for 1,1,1-trichloroethane was greater than the highest exposure concentration, 530,000 µg/l (U.S. EPA, 1978).

For the bluegill, the toxicity of chlorinated ethanes clearly increased as the chlorine content increased. For Daphnia magna, no clear relationship exists, although there is a rough trend toward greater toxicity with increased chlorination. The less chlorinated compounds seem to be more toxic to Daphnia magna than to bluegill, whereas the more heavily chlorinated compounds are more toxic to bluegill.

The Final Acute Values are: 1,2-dichloroethane - 8,800 µg/l, 1,1,2-trichloroethane - 710 µg/l, 1,1,1,2-tetrachloroethane - 960 µg/l, 1,1,2,2-tetrachloroethane - 380 µg/l, all based on Daphnia magna data. The Final Acute Values for pentachloroethane and

hexachloroethane are 1,000 and 140 µg/l, respectively, based on bluegill data. No invertebrate data are available for 1,1,1-trichloroethane and its Final Acute Value, 12,000 µg/l, is based on the fathead minnow and bluegill data.

Chronic Toxicity

No chronic toxicity data are available for fish or invertebrate species.

Plant Effects

Ninety-six-hour EC50 tests, using chlorophyll a and cell number as measured responses, were conducted with the green alga, Selenastrum capricornutum, with the following results (Table 3): 1,1,2,2-tetrachloroethane - 136,000 and 146,000 µg/l, respectively, pentachloroethane - 121,000 and 134,000 µg/l, respectively; and hexachloroethane - 87,000 and 93,200 µg/l. The highest concentration of 1,1,1-trichloroethane tested, 669,000 µg/l, (U.S. EPA, 1978) was not high enough to produce a 96-hour EC50 value (Table 5).

The effects of chlorinated ethanes on plants increased slightly as chlorination increased, but the effect was not as clear as demonstrated by the bluegill data. The alga was approximately 7 to 15 times less sensitive than bluegill to a specific compound. The Final Plant Values are: 136,000 µg/l for 1,1,2,2-tetrachloroethane, 121,000 µg/l for pentacloroethane, and 87,000 µg/l for hexachloroethane.

Residues

The chlorinated ethanes do not strongly bioconcentrate (Table 4), but do show an increased bioconcentration potential with increased chlorination particularly for penta- and hexachloroethane.

The following steady-state bioconcentration factors were measured for bluegill: 1,2- dichloroethane - 2 (14 days); 1,1,1-trichloroethane - 9 (28 days); 1,1,2,2-tetrachloroethane - 8 (14 days); pentachloroethane - 67 (14 days); and hexachloroethane - 139 (28 days). All of the chlorinated ethanes have an elimination half-life of less than two days as measured by whole body levels in exposed bluegill.

No measured steady-state bioconcentration factors (BCF) are available for 1,1,2-trichloroethane and 1,1,1,2-tetrachloroethane. BCFs can be estimated using the octanol-water partition coefficients of 117 and 457, respectively. These coefficients are used to derive estimated BCFs of 22 and 62 for 1,1,2-trichloroethane and 1,1,1,2-tetrachloroethane, respectively, and aquatic organisms that contain about 8 percent lipids. If it is known that the diet of the wildlife of concern contains a significantly different lipid content, appropriate adjustments in the estimated BCFs should be made.

Miscellaneous

All available and pertinent data were discused previously.

CRITERION FORMULATION

Freshwater-Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

1,2-dichloroethane

Final Fish Acute Value = 68,000 µg/l

Final Invertebrate Acute Value = 8,800 µg/l

Final Acute Value = 8,800 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = not available

Residue Limited Toxicant Concentration = not available

Final Chronic Value = not available

0.44 x Final Acute Value = 3,900 µg/l

1,1,1-trichloroethane

Final Fish Acute Value = 12,000 µg/l

Final Invertebrate Acute Value = not available

Final Acute Value = 12,000 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = not available

Residue Limited Toxicant Concentration = not available

Final Chronic Value = not available

0.44 x Final Acute Value = 5,300 µg/l

1,1,2-trichloroethane

Final Fish Acute Value = 5,700 µg/l

Final Invertebrate Acute Value = 710 µg/l

Final Acute Value = 710 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = not available

Residue Limited Toxicant Concentration = not available

Final Chronic Value = not available

0.44 x Final Acute Value = 310 µg/l

1,1,1,2-tetrachloroethane

Final Fish Acute Value = 2,700 µg/l

Final Invertebrate Acute Value = 960 µg/l

Final Acute Value = 960 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = not available

Residue Limited Toxicant Concentration = not available

Final Chronic Value = not available

0.44 x Final Acute Value = 420 µg/l

1,1,2,2-tetrachloroethane

Final Fish Acute Value = 3,000 µg/l

Final Invertebrate Acute Value = 380 µg/l

Final Acute Value = 380 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 140,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 140,000 µg/l

0.44 x Final Acute Value = 170 µg/l

Pentachloroethane

Final Fish Acute Value = 1,000 µg/l

Final Invertebrate Acute Value = 2,500 µg/l

Final Acute Value = 1,000 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 120,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 120,000 µg/l

0.44 x Final Acute Value = 440 µg/l

Hexachloroethane

Final Fish Acute Value = 140 µg/l

Final Invertebrate Acuce Value = 330 µg/l

Final Acute Value = 140 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 87,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 87,000 µg/l

0.44 x Final Acute Value = 62 µg/l

No freshwater criterion can be derived for any chlorinated ethane using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

However, data for pentachloroethane and saltwater organisms can be used as the basis for estimating criteria.

For pentachloroethane and saltwater organisms, 0.44 times the Final Acute Value is less than the Final Chronic Value derived

from a life cycle test with the musid shrimp. Therefore, a reasonable estimate of criteria for other chlorinated ethanes and freshwater organisms would be 0.44 times the Final Acute Value.

1,2-dichloroethane

The maximum concentration of 1,2-dichloroethane is the Final Acute Value of 8,800 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 1,2-dichloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 3,900 µg/l as a 24-hour average and the concentration should not exceed 8,800 µg/l at any time.

1,1,1-trichloroethane

The maximum concentration of 1,1,1-trichloroethane is the Final Acute Value of 12,000 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 1,1,1-trichloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 5,300 µg/l as a 24-hour average and the concentration should not exceed 12,000 µg/l at any time.

1,1,2-trichloroethane

The maximum concentration of 1,1,2-trichloroethane is the Final Acute Value of 710 µg/l and the estimated 24-hour average

concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 1,1,2-trichloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 310 µg/l as a 24-hour average and the concentration should not exceed 710 µg/l at any time.

1,1,1,2-tetrachloroethane

The maximum concentration of 1,1,1,2-tetrachloroethane is the Final Acute Value of 960 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 1,1,1,2-tetrachloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 420 µg/l as a 24-hour average and the concentration should not exceed 960 µg/l at any time.

1,1,2,2-tetrachloroethane

The maximum concentration of 1,1,2,2-tetrachloroethane is the Final Acute Value of 380 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 1,1,2,2-tetrachloroethane the criterion to protect freshwater aquatic life as derived using procedures other

than the Guidelines is 170 µg/l as a 24-hour average and the concentration should not exceed 380 µg/l at any time.

Pentachloroethane

The maximum concentration of pentachloroethane is the Final Acute Value of 1,000 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For pentachloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 440 µg/l as a 24-hour average and the concentration should not exceed 1,000 µg/l at any time.

Hexachloroethane

The maximum concentration of hexachloroethane is the Final Acute Value of 140 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For hexachloroethane the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 62 µg/l as a 24-hour average and the concentration should not exceed 140 µg/l at any time.

Table 1. Freshwater fish acute values for chlorinated ethanes

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Fathead minnow, Pimephales promelas	S	U	1,1,1-trichloroethane	96	105,000	57,404	Alexander, et al. 1978
Fathead minnow, Pimephales promelas	FT	M	1,1,1-trichloroethane	96	52,800	52,800	Alexander, et al. 1978
Bluegill, Lepomis macrochirus	S	U	1,2-dichloroethane	96	550,000	300,000	Dawson, et al. 1977
Bluegill, Lepomis macrochirus	S	U	1,2-dichloroethane	96	431,000	236,000	U.S. EPA, 1978
Bluegill, Lepomis macrochirus	S	U	1,1,1-trichloroethane	96	69,700	38,100	U.S. EPA, 1978
Bluegill, Lepomis macrochirus	S	U	1,1,2-trichloroethane	96	40,200	22,000	U.S. EPA, 1978
Bluegill, Lepomis macrochirus	S	U	1,1,1,2-tetrachloroethane	96	19,600	10,700	U.S. EPA, 1978
Bluegill, Lepomis macrochirus	S	U	1,1,2,2-tetrachloroethane	96	21,300	11,600	U.S. EPA, 1978
Bluegill, Lepomis macrochirus	S	U	Pentachloroethane	96	7,240	3,960	U.S. EPA, 1978
Bluegill, Lepomis macrochirus	S	U	Hexachloroethane	96	980	540	U.S. EPA, 1978

* S = static, FT = flow-through

** U = unmeasured, M = measured

Geometric mean of adjusted values:

1,2-dichloroethane = 266,000 µg/l $\frac{266,000}{3.9}$ = 68,000 µg/l

1,1,1-trichloroethane = 45,799 µg/l $\frac{45,799}{3.9}$ = 12,000 µg/l

1,1,2-trichloroethane = 22,000 µg/l $\frac{22,000}{3.9}$ = 5,700 µg/l

1,1,1,2-tetrachloroethane = 10,700 µg/l $\frac{10,700}{3.9}$ = 2,700 µg/l

1,1,2,2-tetrachloroethane = 11,600 µg/l $\frac{11,600}{3.9}$ = 3,000 µg/l

Pentachloroethane = 3,960 µg/l $\frac{3,960}{3.9}$ = 1,000 µg/l

Hexachloroethane = 540 µg/l $\frac{540}{3.9}$ = 140 µg/l

Table 2. Freshwater invertebrate acute values for chlorinated ethanes (U.S. EPA, 1978)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (µg/l)	Adjusted LC50 (µg/l)	Reference
Cladoceran, Daphnia magna	S	U	1,2-dichloro-ethane	48	218,000	185,000	
Cladoceran, Daphnia magna	S	U	1,1,2-trichloro-ethane	48	18,000	15,000	
Cladoceran, Daphnia magna	S	U	1,1,1,2-tetra-chloroethane	48	23,900	20,200	
Cladoceran, Daphnia magna	S	U	1,1,2,2-tetra-chloroethane	48	9,320	7,890	
Cladoceran, Daphnia magna	S	U	Pentachloro-ethane	48	62,900	53,300	
Cladoceran, Daphnia magna	S	U	Hexachloro-ethane	48	8,070	6,840	

* S = static

** U = unmeasured

Geometric mean of adjusted values: 1,2-dichloroethane = 185,000 µg/l $\frac{185,000}{21}$ = 8,800 µg/l

1,1,2-trichloroethane = 15,000 µg/l $\frac{15,000}{21}$ = 710 µg/l

1,1,1,2-tetrachloroethane = 20,200 µg/l $\frac{20,200}{21}$ = 960 µg/l

1,1,2,2-tetrachloroethane = 7,890 µg/l $\frac{7,890}{21}$ = 380 µg/l

Pentachloroethane = 53,300 µg/l $\frac{53,300}{21}$ = 2,500 µg/l

Hexachloroethane = 6,840 µg/l $\frac{6,840}{21}$ = 330 µg/l

Table 3. Freshwater plant effects for chlorinated ethanes (U.S. EPA, 1978)

Organism	Effect	Concentration (ug/l)
	1,1,2,2-tetrachloroethane	
Alga, Selenastrum capricornutum	EC50 96-hr chlorophyll a	136,000
Alga, Selenastrum capricornutum	EC50 96-hr cell numbers	146,000
	Pentachloroethane	
Alga, Selenastrum capricornutum	EC50 96-hr chlorophyll a	121,000
Alga, Selenastrum capricornutum	EC50 96-hr cell numbers	134,000
	Hexachloroethane	
Alga, Selenastrum capricornutum	EC50 96-hr chlorophyll a	87,000
Alga, Selenastrum capricornutum	EC50 96-hr cell numbers	93,200

Lowest plant value: 1,1,2,2-tetrachloroethane = 136,000 µg/l

Pentachloroethane = 121,000 µg/l

Hexachloroethane = 87,000 µg/l

Table 4. Freshwater residues for chlorinated ethanes (U.S. EPA, 1978)

Organism	Bioconcentration Factor	Time (days)
	1,2-dichloroethane	
Bluegill, Lepomis macrochirus	2	14
	1,1,1-trichloroethane	
Bluegill, Lepomis macrochirus	9	28
	1,1,2,2-tetrachloroethane	
Bluegill, Lepomis macrochirus	8	14
	Pentachloroethane	
Bluegill, Lepomis macrochirus	67	14
	Hexachloroethane	
Bluegill, Lepomis macrochirus	139	28

Table 5. Other freshwater data for chlorinated ethanes (U.S. EPA, 1978)

Organism	Test Duration	Effect	Result (ug/l)
		1,1,1-trichloroethane	
Alga, Selenastrum capricornutum	96 hrs	EC50 chlorophyll a	>669,000
Alga, Selenastrum capricornutum	96 hrs	EC50 cell numbers	>669,000
Cladoceran, Daphnia magna	48 hrs	LC50	>530,000

SALTWATER ORGANISMS

Introduction

The toxicity data base for the 1,2-di-, 1,1,1-tri-, 1,1,2,2-tetra-, penta-, and hexachloroethane to saltwater organisms is limited to an alga, Skeletonema costatum, a mysid shrimp, Mysidopsis bahia, and the sheepshead minnow. Effects of salinity, temperature, or other water quality factors on the toxicity of chlorinated ethanes are unknown.

Acute Toxicity

Toxicity tests with the sheepshead minnow have been conducted with four chlorinated ethanes (Tables 6 and 9). All tests were conducted under static conditions and concentrations in water were not measured. The LC50 values for this saltwater fish do not correlate as well with the number of chlorine atoms as did the values for the bluegill, Lepomis macrochirus (Table 1). When sensitivities of the bluegill and sheepshead minnow are compared to each of these chlorinated ethanes, the LC50 values differ by less than a factor of three, except for pentachloroethane values which differ by a factor of 16. The adjusted 96-hour LC50 values for sheepshead minnows ranged from 1,312 µg/l for hexachloroethane to 63,417 µg/l for pentachloroethane. Since only one test was completed with each chemical, when the adjusted LC50 values are divided by the sensitivity factor (3.7), the following Final Acute Values are obtained: hexachloroethane, 350 µg/l; pentachloroethane, 17,000 µg/l; 1,1,2,2-tetrachloroethane, 1,800 µg/l; 1,1,1,-trichloroethane, 10,000 µg/l.

Mysidopsis bahia, the only invertebrate species tested in static acute tests, and sheepshead minnows were similar in their

sensitivites to the chlorinated ethanes tested, except for pentachloroethane (Table 7). For pentachloroethane and hexachloroethane, the LC50 values for mysid shrimp were lower than those for the freshwater species, Daphnia magna, a cladoceran, (Tables 2 and 7). Sensitivity to chlorinated ethanes increased as the amount of chlorine increased and, generally, this trend occurred also with the freshwater and saltwater invertebrate and fish species. When the adjusted LC50 values for each of the five compounds tested with Mysidopsis bahia are divided by the species sensitivity factor of 49, the Final Invertebrate Acute Values are: hexachloroethane, 16 µg/l; pentachloroethane, 87 µg/l; 1,1,2,2- tetrachloroethane, 160 µg/l; 1,1,1-trichloroethane, 540 µg/l; and 1,2-dichloroethane, 2,000 µg/l. These are also the Final Acute Values since they are lower than the equivalent values for fish.

Chronic Toxicity

Only one chronic value is available for any chlorinated ethane and saltwater organisms. The chronic value for the mysid shrimp and pentachloroethane is 580 µg/l (Table 8). The Final Invertebrate Chronic Value is 110 µg/l, which is obtained by dividing the chronic value by the species sensitivity factor of 5.1. Since no chronic data for saltwater fish are available, 110 µg/l also becomes the Final Chronic Value for pentachloroethane.

Plant Effects

The saltwater alga, Skeletonema costatum, was as sensitive to 1,1,2,2-tetrachloroethane as the mysid shrimp and sheepshead minnow (Table 9). The 96-hour EC50 value for growth, based on cell count, was 6,230 µg/l. The Final Plant Values for pentachloroethane and hexachloroethane, based on the same algal species, are

58,200 and 7,750 µg/l, respectively. There are no data reported in the literature on effects of chlorinated ethanes on saltwater vascular plants.

Miscellaneous

Plant data for 1,2-dichloroethane and 1,1,1-trichloroethane indicate that those compounds are not very toxic to the alga, Skeletonema costatum (Table 10).

CRITERION FORMULATION

Saltwater-Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

1,2-dichloroethane

Final Fish Acute Value = not available

Final Invertebrate Acute Value = 2,000 µg/l

Final Acute Value = 2,000 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = greater than 433,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = greater than 433,000 µg/l

0.44 x Final Acute Value = 880 µg/l

1,1,1-trichloroethane

Final Fish Acute Value = 10,000 µg/l

Final Invertebrate Acute Value = 540 µg/l

Final Acute Value = 540 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = greater than 669,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = greater than 669,000 µg/l

0.44 x Final Acute Value = 240 µg/l

1,1,2,2-tetrachloroethane

Final Fish Acute Value = 1,800 µg/l

Final Invertebrate Acute Value = 160 µg/l

Final Acute Value = 160 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 6,200 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 6,200 µg/l

0.44 x Final Acute Value = 70 µg/l

Pentachloroethane

Final Fish Acute Value = 17,000 µg/l

Final Invertebrate Acute Value = 87 µg/l

Final Acute Value = 87 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = 110 µg/l

Final Plant Value = 58,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 110 µg/l

0.44 x Final Acute Value = 38 µg/l

Hexachloroethane

Final Fish Acute Value = 350 µg/l

Final Invertebrate Acute Value = 16 µg/l

Final Acute Value = 16 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 7,800 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 7,800 µg/l

0.44 x Final Acute Value = 7.0 µg/l

Pentachloroethane

The maximum concentration of pentachloroethane is the Final Acute Value of 87 µg/l and the 24-hour average concentration is the Final Chronic Value of 38 µg/l. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For pentachloroethane the criterion to protect saltwater aquatic life as derived using the Guidelines is 38 µg/l as a 24-hour average and the concentration should not exceed 87 µg/l at any time.

No saltwater criteria can be derived for other chlorinated ethanes using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

However, data for pentachloroethane and saltwater organisms can be used as the basis for estimating criteria.

For pentachloroethane and saltwater organisms, 0.44 times the Final Acute Value is less than the Final Chronic Value derived from a life cycle test with the mysid shrimp. Therefore, a reasonable estimate of criteria for other chlorinated ethanes and saltwater organisms would be 0.44 times the Final Acute Value.

1,2-dichloroethane

The maximum concentration of 1,2-dichloroethane is the Final Acute Value of 2,000 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 1,2-dichloroethane the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 880 µg/l as a 24-hour average and the concentration should not exceed 2,000 µg/l at any time.

1,1,1-trichloroethane

The maximum concentration of 1,1,1-trichloroethane is the Final Acute Value of 540 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 1,1,1-trichloroethane the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 240 µg/l as a 24-hour average and the concentration should not exceed 540 µg/l at any time.

1,1,2,2-tetrachloroethane

The maximum concentration of 1,1,2,2-tetrachloroethane is the Final Acute Value of 160 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 1,1,2,2-tetrachloroethane the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 70 µg/l as a 24-hour average and the concentration should not exceed 160 µg/l at any time.

Hexachloroethane

The maximum concentration of hexachloroethane is the Final Acute Value of 16 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For hexachloroethane the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 7.0 µg/l as a 24-hour average and the concentration should not exceed 16 µg/l at any time.

Table 6. Marine fish acute values for chlorinated ethanes (U.S. EPA, 1978)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)
Sheepshead minnow, Cyprinodon variegatus	S	U	1,1,1-trichloroethane	96	70,900	38,761
Sheepshead minnow, Cyprinodon variegatus	S	U	1,1,2,2-tetrachloroethane	96	12,300	6,724
Sheepshead minnow, Cyprinodon variegatus	S	U	Pentachloroethane	96	116,000	63,417
Sheepshead minnow, Cyprinodon variegatus	S	U	Hexachloroethane	96	2,400	1,312

* S = static

** U = unmeasured

Geometric mean of adjusted values: 1,1,1-trichloroethane = 38,761 µg/l $\frac{38,761}{3.7}$ = 10,000 µg/l

1,1,2,2-tetrachloroethane = 6,724 µg/l $\frac{6,724}{3.7}$ = 1,800 µg/l

Pentachloroethane = 63,417 µg/l $\frac{63,417}{3.7}$ = 17,000 µg/l

Hexachloroethane = 1,312 µg/l $\frac{1,312}{3.7}$ = 350 µg/l

Table 7. Marine invertebrate acute values for chlorinated ethanes (U.S. EPA, 1978)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)
Mysid shrimp, Mysidopsis bahia	S	U	1,2-dichloroethane	96	113,000	95,711
Mysid shrimp, Mysidopsis bahia	S	U	1,1,1-trichloroethane	96	31,200	26,426
Mysid shrimp, Mysidopsis bahia	S	U	1,1,2,2-tetrachloroethane	96	9,020	7,640
Mysid shrimp, Mysidopsis bahia	S	U	Pentachloroethane	96	5,060	4,286
Mysid shrimp, Mysidopsis bahia	S	U	Hexachloroethane	96	940	796

* S = static

** U = unmeasured

Geometric mean of adjusted values: 1,2-dichloroethane = 95,711 µg/l $\frac{95,711}{49}$ = 2,000 µg/l

1,1,1-trichloroethane = 26,426 µg/l $\frac{26,426}{49}$ = 540 µg/l

1,1,2,2-tetrachloroethane = 7,640 µg/l $\frac{7,640}{49}$ = 160 µg/l

Pentachloroethane = 4,286 µg/l $\frac{4,286}{49}$ = 87 µg/l

Hexachloroethane = 796 µg/l $\frac{796}{49}$ = 16 µg/l

Table 8. Marine invertebrate chronic values for chlorinated ethanes (U.S. EPA, 1978)

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)
Mysid shrimp, Mysidopsis bahia	LC	530-630**	580**

* LC = life cycle or partial life cycle

**Data are for pentachloroethane

Geometric mean of chronic values = 580 µg/l $\quad \frac{580}{5.1} = 110$ µg/l

Lowest chronic value = 580 µg/l

Table 9. Marine plant effects for chlorinated ethanes (U.S. EPA, 1978)

Organism	Effect	Concentration (ug/l)
		1,1,2,2-tetrachloroethane
Alga, Skeletonema costatum	EC50 96-hr chlorophyll a	6,440
Alga, Skeletonema costatum	EC50 96-hr cell count	6,230
		Pentachloroethane
Alga, Skeletonema costatum	EC50 96-hr chlorophyll a	58,200
Alga, Skeletonema costatum	EC50 96-hr cell count	58,200
		Hexachloroethane
Alga, Skeletonema costatum	EC50 96-hr chlorophyll a	8,570
Alga, Skeletonema costatum	EC50 96-hr cell count	7,750

Lowest plant value: 1,1,2,2-tetrachloroethane = 6,230 µg/l

Pentachloroethane = 58,200 µg/l

Hexachloroethane = 7,750 µg/l

Table 10. Other marine data for chlorinated ethanes (U.S. EPA, 1978)

Organism	Test Duration	Effect	Result (ug/l)
		1,2-dichloroethane	
Alga, *Skeletonema costatum*	96 hrs	EC50 chlorophyll *a*	>433,000
Alga, *Skeletonema costatum*	96 hrs	EC50 cell count	>433,000
Sheepshead minnow, *Cyprinodon variegatus*	96 hrs	LC50	>126,000 <226,000
		1,1,1-trichloroethane	
Alga, *Skeletonema costatum*	96 hrs	EC50 chlorophyll *a*	>669,000
Alga, *Skeletonema costatum*	96 hrs	EC50 cell count	>669,000

CHLORINATED ETHANES

REFERENCES

Alexander, H.C., et al. 1978. Toxicity of perchloroethylene, trichloroethylene, 1,1,1-trichloroethane, and methylene chloride to fathead minnows. Bull. Environ. Contam. Toxicol. 20: 344.

Dawson, G.W., et al. 1977. The toxicity of 47 industrial chemicals tc fresh and saltwater fishes. Jour. Hazard. Mater. 303.

U.S. EPA. 1978. In-depth studies on health and environmental impacts of selected water pollutants. U.S. Environ. Prot. Agency, Contract No. 68-01-4646.

Mammalian Toxicology and Human Health Effects

EXPOSURE

Introduction

Chloroethanes are hydrocarbons in which one or more of the hydrogen atoms have been replaced by a chlorine atom or atoms. Chloroethanes are widely used because of their low cost and properties which make them excellent solvents, degreasing agents, fumigants and cutting fluids. Some are used in the manufacture of plastics, textiles and in the synthesis of other chemicals. About 1955, chloroethanes began to replace more toxic industrial solvents.

A large number of humans are industrially exposed to chloroethanes. In addition, the general population encounters these compounds in commercial products and as environmental contaminants resulting from industrial emissions including the discharge of liquid wastes.

An extensive literature has been generated by investigators who have studied the effects of chloroethanes on biological systems and the distribution of these compounds in the environment. The use of similar names for related chlorinated hydrocarbons has lead to possible confusion in the literature as to which compound elicited various toxicological effects.

Table 1 indicates the chemical names and some synonyms; Table 2 depicts the chemical structures of the chloroethanes. Chemical and physical properties of chloroethanes are listed in Table 3.

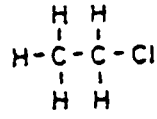
TABLE 1

Chloroethanes and Synonyms

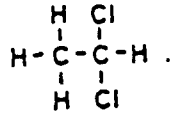
Compound Name	Synonyms	
Monochloroethane	Chloroethane	Ethyl chloride
1,1,-Dichloroethane	Ethylidene Dichloride	Ethylidene Chloride
1,2-Dichloroethane	Ethylene Dichloride	Ethylene Chloride
1,1,1-Trichloroethane	Methyl Chloroform	Chlorothene
1,1,2-Trichloroethane	Ethane Trichloride	Vinyl Trichloride
1,1,1,2-Tetrachloroethane	Tetrachloroethane	
1,1,2,2-Tetrachloroethane	Acetylene Tetrachloride	Sym-Tetrachloroethane
Pentachloroethane	Pentalin	Ethane Pentachloride
Hexachloroethane	Perchloroethane	

TABLE 2

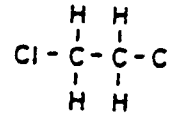
CHLOROETHANES



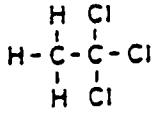
Monochloroethane



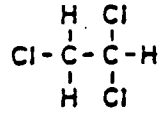
1,1-Dicholoro-ethane



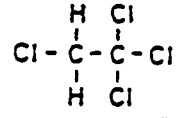
1,2-Dichloro-ethane



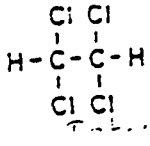
1,1,1-Trichloro-ethane



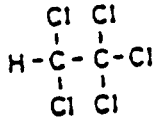
1,1,2-Trichloro-ethane



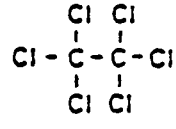
1,1,1,2-Tetra-chloroethane



1,1,2,2-Tetrachloro-ethane



Penta-chloro-ethane



Hexachloro-ethane

TABLE 3

Physical and Chemical Properties of Chloroethanes

Compound	Formula Weight	Boiling Point °C	Melting Point °C	Specific Gravity[a]	Solubility In Water	Vapor Pressure (mm Hg)	Vapor Density[b]
monochloroethane	64.52	13.1	-138.7	0.9214	5.74 g/l	1,000 at 20°C	
1,1-dichloroethane	98.96	57.3	- 98	1.1776	5 g/l	230 at 25°C	
1,2-dichloroethane	98.96	83.4	- 35.4	1.253	8.1 g/l	85 at 25°C	3.42
1,1,1-trichloroethane	133.4	74.1	- 33	1.3492	480 parts per 10^6 w/w	96 at 20°C	4.55
1,1,2-trichloroethane	133.4	113	- 37.4	1.4405	Slightly soluble		
1,1,1,2-tetrachloroethane	167.9	129	- 68.1	1.5532	2.85 g/l		
1,1,2,2-tetrachloro-	167.9	146.3	- 36	1.596	2.9 g/l	16 at 25°C	5.79
pentachloroethane	202.3	162	- 29	1.6796	Insoluble		
hexachloroethane	236.7	186	- 187	2.091	Insoluble		

[a] At 20°C; Water = 1.00 at 4°C

[b] Air = 1.00

References:

Walter, et al. 1976
Price, et al. 1974
Amer. Ind. Hyg. Assoc. 1963; 1956
Weast, 1976

Ingestion from Water

The U.S. Environmental Protection Agency (1974) identified a number of toxic compounds in low concentrations in raw and finished waters of which approximately 38 percent were halogenated (U.S. EPA, 1976). Halogenated hydrocarbons have also been identified in 80 domestic water supplies by Symons, et al. (1975). Bellar, et al. (1974a) observed the highest concentration of organohalides in chlorinated finished water originating from surface water (37 to 150 mg/l). Among the compounds identified in raw or treated water are: 1-2-dichloroethane (Brass, et al. 1977); 1,1,1-trichloroethane, (Kopfler, et al. 1976); in finished water, 1,1- and 1,2-dichloroethane, and 1,1,1-trichloroethane, (Coleman, et al. 1976); 1,1,2-trichloroethane, 1,1,1,2-tetrachloroethane (Keith, et al. 1976). Other reports of halogenated compounds in water or industrial waste water include the following: U.S. EPA., 1975a; Keith, 1972; Dowty, et al. 1975a,b; Bellar, et al. 1974b; Dietz and Iraud, 1973.

Even though individual chemicals are present in relatively small amounts in public water supplies, the toxicological implications are a matter of great concern. Chronic ingestion of chloroethanes may result in synergistic interactions and alterations of basic metabolic pathways (Tardiff, et al. 1978). Of the 289 compounds identified in U.S. drinking water supplies (U.S. EPA, 1976), 21 have been characterized as having carcinogenic activity (Kraybill, 1978). Of these 21, three are chloroethanes: 1,2-dichloroethane; 1,1,2-

trichloroethane; tetrachloroethane (isomer not identified). Studies of Harris and Epstein (1976) suggested there is an epidemiologic link between the presence of halogenated organic compounds in drinking water and the incidence of cancer in populations along the lower Mississippi River, where contamination is particularly high.

Monochloroethane is widely used as a solvent and in chemical synthesis (Natl. Inst. Occup. Safety Health, 1978c). No literature was found indicating the amounts discharged as liquid industrial wastes; however, chloroethane has been identified in finished water supplies (Kopfler, 1976). Brown, et al. (1975) reported that from six companies producing monochloroethane 5.8 million pounds per year were lost into the environment from 575.5 million pounds produced; major losses would be into the atmosphere. Due to its low solubility in water (5.74 g/l), monochloroethane would be present only in water near point sources. In surface waters above 12.3°C the compound would volatilize into the atmosphere.

1,1-Dichloroethane is not reported to be produced commercially in the United States (Natl. Inst. Occup. Safety Health, 1978c), but is imported for use as a solvent and cleaning agent in specialized processes. 1,1-Dichloroethane has been identified in the finished water of several metropolitan areas (Coleman, et al. 1976; Kopfler, et al. 1976).

More than 80 percent of the 1,2-dichloroethane produced in the United States is converted to vinyl chloride and other chlorinated chemicals (U.S. EPA, 1975b); the solvent is also used in the manufacture of tetraethyl lead and as

a constituent of many products used by the general public (U.S. EPA, 1975a). The gross annual discharge of 1,2-dichloroethane was estimated at 80 tons by the U.S. EPA (1975a). Nonpoint sources result from the use of products containing 1,2-dichloroethane such as paint, varnish, and finish removers. The compound is difficult to degrade biologically (Price, et al. 1974), however, activated carbon filtration is 90 to 100 percent effective in removing the solvent from finished water (U.S. EPA, 1975a). Of 80 water supplies surveyed, 27 contained 1,2-dichloroethane at concentrations of 0.2 to 8 ug/l. (U.S. EPA, 1975c, 1974).

1,1,1-Trichloroethane is used primarily as a solvent, cleaning, and degreasing agent (Dow Chemical Co. 1969; 1973). The compound was found in the drinking water of three of five cities studied by Kopfler, et al. (1976). No information was found of the environmental fate in water or estimates of annual discharge as waste.

1,1,2-Trichloroethane is used in the manufacture of 1,1-dichloroethylene, as a solvent, and in organic synthesis. The gross annual discharge is estimated at 2,000 tons. The compound is not produced by the biological decomposition of sewage or solid wastes or by incineration, but small amounts are formed by the chlorination process. 1,1,2-Trichloroethane persists in the environment (greater than 2 years) and is not degraded biologically; however, activated carbon filtration is reported to be 90 to 100 percent effective in removing the chloroethane from drinking water (U.S. EPA, 1975a). Of 10 water supplies surveyed by the U.S. EPA (1975a), only one contained 1,1,2-trichloroethane, while a second

study of finished water of a metropolitan area, reported concentrations of 0.1 to 8.5 µg/l (U.S. EPA, 1975d).

1,1,1,2-Tetrachloroethane is used as a solvent and in the manufacture of a number of widely used products, (U.S. EPA, 1975a). It is potentially formed during chlorination of water (U.S. EPA, 1975a) and has been identified in finished water at a concentration of 0.11 µg/l (U.S. EPA, 1974).

1,1,2,2-Tetrachloroethane is used in the manufacture of 1,1-dichloroethylene, as a solvent, in the manufacture of, and as a constituent of many widely used products. The gross annual discharge from industrial sources was estimated to be 2,000 tons. The compound is not formed during biological decomposition of sewage or solid waste or by incineration, but may be formed during chlorination of treated sewage. The compound persists in the environment and is not degraded biologically but can be removed from drinking water by activated carbon filtration which is reported to be 90 to 100 percent effective (U.S. EPA, 1975a).

Apparently pentachloroethane is not produced commercially in the United States (Natl. Inst. Occup. Safety Health, 1978c) and is rarely found in drinking water.

Hexachloroethane is used in the manufacture of a number of products and the gross annual industrial discharge is estimated at 2,000 tons. It is not formed in biological decomposition of wastes but can be produced in small quantities by chlorination of drinking water. The compound persists in the environment and is not degraded biologically (U.S. EPA, 1975a).

Analytical Techniques: Sensitive methods for identification of chlorinated ethanes and other organic compounds found in water, methods of quantitation, efficiency of sampling techniques and recovery were discussed by Keith, et al. (1976). Computerized gas chromatography/mass spectroscopy was presented as the best method available. There are many recent publications describing water sampling and analytical techniques for the identification of halogenated aliphatic hydrocarbons including the following: Dowty, et al. 1975b; Van Rossum and Webb, 1978; Lillian and Singh, 1974; Gough, et al. 1978; Glaze, et al. 1976; Deetman, et al. 1976; Coleman, et al. 1976; Fujii, 1977; Kopfler, et al. 1976; Cavallaro and Grassi, 1976; Nicholson and Meresz, 1975.

Ingestion from Food

The two most widely used solvents, 1,2-dichloroethane and 1,1,1-trichloroethane, are most often found in food. 1,1,1-Trichloroethane was found in small amounts as a contaminant in various food stuffs from the United Kingdom (Walter, et al. 1976). In meat, oils and fats, tea, and fruits and vegetables, amounts ranged from 1 to 10 ug/kg. Of the foods analyzed, olive oil contained the largest amount (10 ug/kg).

1,2-Dichloroethane is used in washing or lye peeling of fruits and vegetables (42 FR 29856) and represents a possible source in the diet of man. The volatile compound is also used as a fumigant in the storage of grain; however, residues of 1,2-dichloroethane were not detected in wheat, flour, bran, middlings, and bread (Berck, 1974).

1,2-Dichloroethane is commonly used as an extractant in the preparation of spice oleoresins. The dichloroethane isomer was detected in 11 of 17 spices in concentrations ranging from 2 to 23 ug solvent per gram spice oleoresin (Page and Kennedy, 1975).

Concentrations of seven halogenated hydrocarbons were determined in various organs of three species of molluscs and five species of fish (Dickson and Riley, 1976). 1,1,1-Trichloroethane was found in the digestive tissue of one mollusc species (4 ng/g on a dry weight basis), and in three fish species where the compound was most strongly concentrated in the brain (4 to 16 ng) and gills (2 to 14 ng).

No other data were found concerning the biological fate of chloroethanes in the food chain. The specific gravities of chloroethanes (except monochloroethane) would tend to maximize effects in the bottom of streams or other bodies of water. The amount present which could be incorporated in the food chain would be limited by the solubility of the solvents in water (Table 3).

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms, but BCF's are not available for the edible portions of all four major groups of aquatic organisms consumed in the United States. Since data indicate that the BCF for lipid-soluble compounds is proportional to percent lipids, BCF's can be adjusted to edible portions using data on percent lipids and the amounts of various species consumed by Americans. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita

consumption is 18.7 g/day. From the data on the nineteen major species identified in the survey and data on the fat content of the edible portion of these species (Sidwell, et al. 1974), the relative consumption of the four major groups and the weighted average percent lipids for each group can be calculated:

Group	Consumption (Percent)	Weighted Average Percent Lipids
Freshwater fishes	12	4.8
Saltwater fishes	61	2.3
Saltwater molluscs	9	1.2
Saltwater decapods	18	1.2

Using the percentages for consumption and lipids for each of these groups, the weighted average percent lipids is 2.3 for consumed fish and shellfish.

Measured steady-state bioconcentration factors of 2, 9, 8, 67, and 139 were obtained for 1,2-dichloroethane, 1,1,1-trichloroethane, 1,1,2,2-tetrachloroethane, pentachloroethane, and hexachloroethane, respectively using bluegills containing about one percent lipids (U.S. EPA, 1978). An adjustment factor of 2.3/1.0 = 2.3 can be used to adjust the measured BCF from the 1.0 percent lipids of the bluegill to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factors for 1,2-dichloroethane, 1,1,1-trichloroethane, 1,1,2,2-tetrachloroethane, pentachloroethane, and hexachloroethane and the edible portion of all aquatic organisms consumed by Americans are calculated to be 4.6, 21, 18, 150, and 320, respectively.

No measured steady-state bioconcentration factors (BCF) are available for 1,1,2-trichloroethane and 1,1,1,2-tetrachloroethane, but the equation "Log BCF = 0.76 Log P - 0.23" can be used (Veith, et al. Manuscript) to estimate the BCF for aquatic organisms that contain about eight percent lipids from the octanol-water partition coefficient (P). Based on octanol-water partition coefficients of 117 and 457, respectively, the steady-state bioconcentration factors for 1,1,2-trichloroethane and 1,1,1,2-tetrachloroethane are estimated to be 22 and 62. An adjustment factor of 2.3/8.0 = 0.2875 can be used to adjust the estimated BCF from the 8.0 percent lipids on which the equation is based to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factors for 1,1,2-trichloroethane and 1,1,1,2-tetrachloroethane and the edible portion of all aquatic organisms consumed by Americans is calculated to be 6.3 and 18, respectively.

Inhalation

Inhalation is the major route of exposure of humans to the volatile chloroethanes which are widely used as solvents, particularly in metal degreasing and dry cleaning operations. Many tons are reported to evaporate into the atmosphere (Kover, 1975; Murray and Riley, 1973). Inhalation exposure data for the general population are not available; however, some estimates can be made for occupational exposures. For example, health hazard evaluations of industries using 1,1,1-trichloroethane reported breathing zone concentrations ranging from 1.5 to 396 ppm (Table 4).

TABLE 4

Concentrations of 1,1,1-Trichloroethane
Observed in Ambient Air of Various Industries

Concentrate Range (ppm)	Type of Job or Industry	Reference
4.0 - 37.0	Machining, Degreasing	Kominsky, 1976
2.5 - 79.5	Electrical Industry	Gilles, 1976
6.0 - 83.0	Electrical Industry	Gilles & Philbin, 1976
2.0 - 18.4	Manufacture Catapult Cylinders	Gilles & Rostand, 1975
36.5 - 159.5	Manufacture Rifle Scopes	Gunter, et al. 1977
73.0 - 350.0	Degreasing-Cleaning	Gilles, 1977
1.5 - 16.6	Metal Industry	Levy & Meyer, 1977
12.0 - 118.0	Soldering-Degreasing	Gunter & Bodner, 1974

Dermal

Normally the skin is not a major route of exposure. As with most solvents, chloroethanes are absorbed through the skin, but in general, skin contact is avoided in the workplace and commercial products carry warnings. Most laboratory gloves are permeable to these solvents and should not be relied upon for protection (Sansone and Tewari, 1978).

PHARMACOKINETICS

Absc ption

Monochloroethane is absorbed rapidly into the body following ingestion or inhalation (Sax, 1975) and has been used as an anesthetic (Merck, 1976). Absorption through the skin is minor.

Lethal amounts of 1,2-dichloroethane are absorbed following ingestion of a single dose (LD50 for rats, 0.77 m/l/kg) or a single application to the skin (LD50 for rabbits, 3.89 mg/kg) (Smyth, et al. 1969). According to NIOSH (1978a) the effects of large doses of 1,2-dichloroethane are similar for all routes of entry. Absorption of 1,1-dichloroethane is similar to that of the 1,2-isomer; however, the 1,1-isomer is less toxic.

Absorption of liquid 1,1,1-trichloroethane through the skin was studied by Stewart and Dodd (1964). Six subjects each immersed a thumb in a beaker of 1,1,1-trichloroethane for 30 minutes. Analysis of samples collected at 10, 20 and 30 minutes indicated slow absorption (Table 5). In the workplace, concern for toxic effects resulting from skin contact with 1,1,1-trichloroethane is usually one of dermatitis (Gilles, 1977). The concentration of 1,1,1-trichloroethane in the blood of victims of fatal intoxication (ingested or inhaled) has been reported to be 60, 62, and 120 ppm (Stahl, et al. 1969) indicating rapid absorption by both routes.

TABLE 5

Concentrations of 1,1,1-Trichloroethane Found in Alveolar Air of Experimental Subjects

Duration of Thumb Immersion	Alveolar Air Concentrations (ppm)
10 minutes	0.10 - 0.10
20 minutes	0.14 - 0.37
30 minutes	0.19 - 1.02

Source: Stewart and Dodd, 1964

1,1,2-Trichloroethane is absorbed more rapidly following ingestion or inhalation than following a dermal exposure as indicated by LD50s. A dermal LD50 for 1,1,2-trichloroethane was reported for rabbits to be 3.73 ml/kg body weight; an ingestion LD50 for rats was reported to be 0.58 ml/kg, for inhalation, an 8-hour exposure at 500 ppm was fatal to four of six rats (Smyth, et al. 1969). A single application of 1 ml of pure solvent to the skin of guinea pigs was absorbed rapidly as indicated by the appearance of 3 to 4 µg/ml of the solvent in the blood in 30 minutes. After 12 hours, the blood concentration rose to almost 5 µg/ml (Jakobson, et al. 1977).

The absorption of inhaled 1,1,2,2-tetrachloroethane in humans was determined by Morgan, et al. (1970, 1972) using ^{38}Cl-labeled 1,1,2,2-tetrachloroethane. Volunteers deeply inhaled 2.5 mg of labeled vapor, held their breath for 20 seconds, exhaled through an activated-charcoal trap, inhaled room air, then exhaled through the trap a second time. Ninety-four to 97 percent of the inhaled tetrachloro-

ethane was retained. Subjects continued to breathe room air and exhale for one hour through charcoal traps. Only 3.3 to 6 percent of the initially retained vapor (as ^{38}Cl) was exhaled one hour after the single inhalation exposure. Carbon dioxide was not monitored. Of a number of halogenated hydrocarbons tested (Morgan, et al. 1972), 1,1,2,2-tetrachloroethane had the highest partition coefficient, one of the highest rates of absorption (lungs) and one of the lowest rates of elimination by exhalation.

Distribution

In studying the metabolism of chloroethanes, Yllner (1971a,b,c,d,e) reported that a small amount of an intraperitoneal (i.p.) dose of 1,2-dichloroethane (0.05 to 0.17 g/kg/body weight) administered to mice was retained after 3 days, 0.6 to 1.3 percent of the dose administered. One to 3 percent of a dose of 1,1,2-dichloroethane (0.1 to 0.2 g/kg) was retained after 3 days. The highly toxic 1,1,2,2-tetrachloroethane (0.21 to 0.32 g/kg) was metabolized more slowly or stored, since 16 percent of the dose was retained 3 days after the dose was injected i.p. (Yllner, 1971d).

Holmberg, et al. (1977), studied the distribution of 1,1,1-trichloroethane in mice during and after inhalation. Solvent concentrations in the kidney and brain were about the same at a given exposure concentration, but concentrations in the liver were twice those observed in the kidney and brain following exposures to 100 ppm or more (Table 6). A pharmacokinetic model with both uptake and elimination of the first order best fitted the empirical data. Hake, et al. (1960) reported that 0.09 percent of a large dose

of 1,1,1-trichloroethane was retained in the skin of rats as the parent compound 25 hours after administration of an i.p. dose (~700 mg per kg). The blood contained 0.02 percent, the fat 0.02 percent, and other sites 0.1 percent of the dose administered.

A study of solvents in post mortem human tissue was reported by Walter, et al. 1976. 1,1,1-Trichloroethane was found in body fat (highest concentration), kidney, liver, and brain. Data from autopsies of humans dying from acute exposures indicate that the highest tissue concentration was in the liver, followed by brain, kidney, muscle, lung, and blood (Stahl, et al. 1969).

In pregnant rats and rabbits, inhalation or ingestion of 1,1,1,2-tetrachloroethane resulted in the presence of high levels of the solvent in the fetuses (Truhaut, et al. 1974).

TABLE 6

Concentrations of 1,1,1-Trichloroethane in Tissues of Mice Following Inhalation Exposures

Concentration (ppm)	Exposure Time (h)	ug 1,1,1-Trichloroethane/g Tissue			
		Blood	Liver	Kidney	Brain
10	24	0.6 ± 0.16[a]	1.5 ± 0.3	1.1 ± 0.2	0.8 ± 0.1
100	24	6.3 ± 3.0	12.2 ± 4.6	5.9 ± 2.2	6.2 ± 1.3
1,000	6	36 ± 16	107 ± 38	60 ± 16	57 ± 17
5,000	3	165 ± 25	754 ± 226	153 ± 27	156 ± 24
10,000	6	404 ± 158	1429 ± 418	752 ± 251	739 ± 170

[a]Values are means and standard deviations from 4 to 10 animals.
Source: Holmberg, et al. 1977

Metabolism (In Vivo)

In 1971, Yllner published a series of papers dealing with the metabolism of chloroethanes. Solvents were injected i.p. into mice and the excretion of metabolites in the urine monitored for three days. Table 7 summarizes Yllner's observations.

Metabolism of the highly toxic 1,1,2,2-tetrachloroethane, based on the identification of ^{14}C-labeled metabolites in the urine of mice (Yllner, 1971d), involved a stepwise hydrolytic cleavage of the chlorine-carbon bonds yielding glyoxalic acid and carbon dioxide. Nonenzymatic oxidation of 1,1,2,2-tetrachloroethane may produce a small amount of tetrachloroethylene. The parent compound may be dehydrochlorinated to form small amounts of trichloroethylene, precursor to trichloroacetic acid, and trichloroethanol.

The metabolism of pentachloroethane in the mouse is postulated to proceed at least partly through trichloroethylene and its metabolite chloral hydrate. The latter compound could also be formed from pentachloroethane by hydrolytic fission of carbon-chlorine bonds (Yllner, 1971e).

In Yllner's experiments, the percentage of the dose metabolized decreased with an increasing dose (1971a,b,c,d,e), suggesting that degradative pathways become saturated and an increasing amount is expired unchanged or retained in the body.

Ikeda and Ohtsuji (1972) exposed rats by inhalation to 200 ppm chloroethanes (1,1,1-tri; 1,1,2-tri; 1,1,1,2-tetra; or 1,1,2,2-tetrachloroethane) for eight hours and

TABLE 7

Major Metabolites of Chloroethanes in Mice

Compound	Dose (g/kg)	Urinary Metabolites		
		Total %	Identified	% of Dose
1,2-Dichloroethane (^{14}C-)	12-15	51-73	S-carboxymethylcysteine	44-46 Free 0.5-5 Bound
			Thiodiacetic acid	33-44
			Chloroacetic acid	6-23
			2-Chloroethanol	0.0-0.8
			S,S'-ethylene-bis-cysteine	0.7-1.0
1,1,2-Trichloroethane (^{14}C-)	10-13	6-9	S-carboxymethylcysteine	29-46 Free 3-10 Bound
			Chloroacetic acid	6-31
			Thiodiacetic acid	38-42
			2,2-Dichloroethanol	
			2,2,2-Trichloroethanol	
			Oxalic acid	
			Trichloroacetic acid	
1,1,1,2-Tetrachloroethane		~17-49	Trichloroethanol	17-49
			Trichloroacetic acid	1-7
1,1,2,2-Tetrachloroethane (^{14}C-)	0.21-0.32	23-34	Dichloroacetic acid	
			Trichloroacetic acid	
			Trichloroethanol	
			Oxalic acid	
			Glyoxylic	
			Urea	
			Half of urinary activity not accounted for	
Pentachloroethane	1.1-1.8		Trichloroethanol	16-32
			Trichloroacetic acid	9-18
			Expired air contained trichloroethylene (2-16%) and tetrachloroethylene (3-9%)	

Source: Yllner, 1971a, b, c, d, and e

collected the urine for 48 hours from the beginning of exposure. Equimolar amounts of the same four solvents were injected i.p. into rats. Metabolites in the urine following inhalation or i.p. administration of all four solvents were trichloroacetic acid (TCA) and trichloroethanol(TCE) (Table 8), although relative amounts varied with the individual solvent. Metabolites were determined colorimetrically by the Fujiwara reaction; trichloroethanol was determined as the difference between the total trichlorocompounds and trichloroacetic acid.

Truhaut (1972) identified metabolites in the urine of rats, rabbits and guinea pigs given oral doses of 1,1,1,2-tetrachloroethane. His results indicate that the solvent is metabolized to trichloroethanol and excreted in the urine as trichloroethyl- -D-glucuronic acid. In rats, small amounts of trichloroacetic acid were also formed.

Van Dyke and Wineman (1971) investigated the enzymatic dechlorination of a series of chloroethanes by rat liver microsomes (Table 9). The system required NADPH and oxygen and was induced by phenobarbitol and benzo(a)pyrene, but not by methylcholanthrene. Dechlorination of 1,1,2-trichloroethane was stimulated by addition of the 100,000 x g supernatant to the microsomal assay (Gandolfi and Van Dyke, 1973).

1,1,2,2-Tetrachloroethane and hexachloroethane (2.6 mmol/kg body weight) administered perorally to rats, decreased the cytochrome P-450 content and overall drug hydroxylation activity in the liver (Vainio, et al. 1976). Working with

TABLE 8

Urinary Metabolites from Wistar Rats Exposed to Solvents

Solvent	No. of Experiments	Urinary Metabolites (mg/kg/body weight) TCA	TCE
Inhalation[a] 200 ppm 8 hrs.			
1,1,1-Trichloroethane	8	0.5 ± 0.2	3.1 ± 1.0
1,1,2-Trichloroethane	8	0.3 ± 0.1	0.3 ± 0.1
1,1,1,2-Tetrachloroethane	8	39.4 ± 5.0	159.6 ± 24.4
1,1,2,2-Tetrachloroethane	8	1.7 ± 0.9	6.5 ± 2.7
Intraperitoneal[b] 2.78 mmol per kg body weight			
1,1,1-Trichloroethane	8	0.5 ± 0.2	3.5 ± 1.4
1,1,2-Trichloroethane	8	0.4 ± 0.1	0.2 ± 0.1
1,1,1,2-Tetrachloroethane	8	16.9 ± 1.6	97.3 ± 8.1
1,1,2,2-Tetrachloroethane	8	1.3 ± 0.2	0.8 ± 0.4

[a]Six rats per group

[b]Five rats per group

Source: Ikeda and Ohtsuji, 1972

TABLE 9

Dechlorination of Chloroethanes by
Rat Liver Microsomes

Compound[a]	Percent ^{35}Cl Enzymatically Removed[b]
Monochloroethane	< 0.5
1,1-Dichloroethane	13.5
1,2-Dichloroethane	< 0.5
1,1,1-Trichloroethane	< 0.5
1,1,2-Trichloroethane	9.8
1,1,1,2-Tetrachloroethane	0.8
1,1,2,2,-Tetrachloroethane	6.0
Pentachloroethane	1.7
Hexachloroethane	3.9

[a]Uniformly labeled with chlorine-36

[b]Results are averages of duplicate assays from at least six rats

Source: Van Dyke and Wineman, 1971

hepatic microsomes isolated from phenobarbital-induced rats, Ivanetich, et al. (1978), found that 1,1,1-trichloroethane and 1,2-dichloroethane degraded the heme moiety of cytochrome P-450; degradation appeared to require metabolic activation since NADPH was a requirement for binding.

In controlled human exposure studies, metabolism of inhaled 1,1,1-trichloroethane (70 ppm for 4 hours) represented 3.5 percent of total uptake (Monster, 1979). The author suggested that transformation of the parent compound takes place by hydroxylation to trichloroethanol, followed by partial oxidation of trichloroethanol to trichloroacetic acid.

Excretion

Yllner quantitated the excretory products of 1,2-di; 1,1,2-tri; 1,1,1,2-tetra; 1,1,2,2-tetra; and penta-chloroethane in mice (1971a,b,c,d,and e) (Table 10). Compounds were administered i.p. and excretion was monitored for 3 days; urinary metabolites are listed in Table 7.

More than 90 percent of the doses of 1,2-dichloroethane or 1,1,2-trichloroethane was excreted in the first 24 hours with more than half found in the urine. Seventy-eight percent of the 1,1,1,2-tetrachloroethane administered was excreted in 72 hours with 48 percent expired unchanged (21 to 62 percent); expired CO_2 was not detected. Eighty-four percent of the 1,1,2,2-tetrachloroethane dose was excreted in 72 hours, with about half the dose excreted as CO_2, and one-fourth in the urine; approximately 16 percent remained in the animal. About one-third of the pentachloroethane dose was expired unchanged; the expired air also contained tri-

TABLE 10

Excretion of Chloroethanes Administered to Mice[a]

Chloroethane Compound	Dose (g/kg)	Expired Unchanged (%)	Expired as CO_2 (%)	In Urine (%)	In Feces (%)
1,2-	0.05-0.17	10-45	12-15	51-73	0-0.6
1,1,2-	0.1 -0.2	6-9	10-13	73-87	0.1-2.0
1,1,1,2-	1.2 -2.0	21-62	-	18-56	-
1,1,2,2-	0.21-0.32	4	45-61	23-34	-
Penta-	1.1 - 1.8	12-51	-	25-50	-

[a]Intraperitoneal injection - Excretory products collected for 3 days

Source: Yllner, (1971a, b, c, d, and e)

chloroethylene (2 to 16 percent) and tetrachloroethylene (3 to 9 percent) indicating dechlorination of pentachloroethane. Twenty-five to 50 percent of the dose was in the urine.

Stewart, et al. (1961, 1969, 1975) studied controlled human exposures to 1,1,1-trichloroethane vapor. The concentration of the unchanged solvent in the post-exposure expired air was predictable enough to estimate the magnitude of exposure. The rate of 1,1,1-trichloroethane excretion was a function of exposure duration as well as concentration (Table 11).

TABLE 11

1,1,1-Trichloroethane Breath Concentrations of
Men and Women Exposed at 350 ppm

Time	Men			Women		
	No.	Mean (ppm)	Range	No.	Mean (ppm)	Range
	Isolated 1-Hour Exposure					
2 Minutes preexit exposure	3	150	144 - 157	3	183	173 - 193
1 Minute post exposure	3	76.4	48.6 - 108	2	120	116 - 123
23 Hours post exposure	3	1.11	0.75 - 1.63	2	0.8	0.57 - 1.03
	Isolated 7.5 Hour Exposure					
2 Minutes preexit exposure	4	234	222 - 252	3	254	247 - 262
1 Minute post exposure	4	149	144 - 153	4	181	156 - 205
16 Hours post exposure	4	7.07	6.62 - 7.73	4	6.93	4.83 - 8.74

Source: Stewart, et al. 1975

Monster, et al. (1979) reported that 60 to 80 percent of 1,1,1-trichloroethane (70 or 140 ppm for 4 hours) inhaled by human volunteers was expired unchanged; two metabolites, trichloroethanol and trichloroacetic acid, excreted in the urine, represented approximately three percent of the total uptake. Although measurements of parent compound and its metabolites are commonly used to estimate uptake of 1,1,1-trichloroethane, studies by Monster and Houtkooper (1979) have shown that the best estimates of uptake are provided by concentrations present in blood.

A multistage cryogenic trapping system was used to concentrate trace organic compounds in human respiratory gas: three chlorinated ethanes - 1,1,1-trichloroethane, 1,1- and 1,2-dichloroethane - were identified in the expired air of subjects with no known history of exposure (Conkle, et al. 1975). No estimates of half-lives and body burdens of chloroethanes were found in the literature. These data must be obtained, however, in order to identify populations at risk.

EFFECTS

Acute, Sub-acute, and Chronic Toxicity

A number of excellent publications are available which review the acute and chronic effects of some chloroethanes. Aviado, et al. (1976) published a monograph on "Methyl Chloroform and Trichloroethylene in the Environment." NIOSH (1978b) published criteria documents for recommended standards of occupational exposure to 1,1,1-trichloroethane (1978b), 1,2-dichloroethane (1976b), and 1,1,2,2-tetrachloroethane (1976a). A monograph prepared by Walter, et al. (1976)

on chlorinated hydrocarbon toxicity, included 1,1,1-trichloroethane and was prepared for the Consumer Product Safety Commission, Bureau of Biomedical Science. A comprehensive review of 1,1,1-trichloroethane literature from 1953 through 1973 was conducted by the Franklin Institute Research Laboratories for the U.S. Environmental Protection Agency (Kover, 1975).

Only a representative portion of the literature available on the toxic effects of chloroethanes will be discussed since the focus of this document is on the effects of chronic ingestion and possible carcinogenic effects.

Monochloroethane is considered one of the least toxic of the chloroethanes; however, as a halogen-containing hydrocarbon it is potentially damaging to the liver and is known to disturb cardiac rhythm (Goodman and Gilman, 1975). Overdoses of several volatile anesthetics including monochloroethane can lead to severe contractile failure of the heart (Doering, 1975). At the stage of maximal failure, the myocardial stores of ATP and phosphocreatine were increased indicating a reduction in the utilization of energy stores.

1,1-Dichloroethane is less toxic than the 1,2-isomer but the 1,1-isomer's use as an anesthetic was discontinued because of marked excitation of the heart (Browning, 1965). Liver injury has been reported in experimental animals (Sax, 1975) following acute exposures ranging from 4,000 to 17,500 ppm.

Smyth, et al.(1969) reported an oral LD50 for 1,2-dichloroethane in rats of 0.77 ml/kg (range 0.67 to 0.89) and a dermal LD50 for rabbits of 3.89 ml/kg (range 3.40 to 4.46). In both cases a single dose was administered.

Acute and subacute inhalation studies with dogs, rabbits, guinea pigs, rats and mice indicated that 1,2-dichloroethane was toxic to the liver, bone marrow, blood, kidneys, myocardium and sometimes the adrenals (Heppel, et al. 1946; Liola, et al. 1959; Liola and Fondacaro, 1959). Chronic inhalation exposures, 100 to 400 ppm, from 5 weeks to 32 weeks in several species were reported to be toxic in the liver at 200 ppm and above (Spencer, et al. 1951; Hofmann, et al. 1971). Increased liver weights were observed in guinea pigs following a 32 week exposure to 100 ppm 1,2-dichloroethane (Spencer, et al. 1951).

A correlation was found between serum ornithine carbamyl transferase (OCT) activity and hepatocellular damage caused by injection (i.p.) of acute doses of solvents (in corn oil) into guinea pigs (Divincenzo and Krasavage, 1974). Of 33 solvents tested, 5 were chlorinated ethanes: 1,1-; 1,2-; 1,1,1-; 1,1,2-; 1,1,2,2-. At 500 mg/kg, 1,2-dichloroethane caused an increase in OCT activity, however, no liver damage was detected histologically. At 200 or 400 mg/kg, 1,1,2-trichloroethane stimulation of OCT activity was not dose related but liver damage was observed histologically. In this study, the remaining solvents (1,1-; 1,1,1-; 1,1,2,2-dichloroethane) did not increase OCT activity nor cause discernable hepatocellular damage.

Ingestion of 1,2-dichloroethane by man has often resulted in death which was usually ascribed to circulatory and respiratory failure. Brief descriptions of several cases are presented in Table 12. In addition to the signs and symptoms listed in Table 12, a reduction in clotting factors and

TABLE 12

Signs and Symptoms Following
1,2-Dichloroethane Ingestion

Author	Patient Data	Amount Consumed	Onset of Symptoms	Progression of Signs and Symptoms
Secchi, et al. (1968)	80-year-old	50 ml		Elevated serum enzymes--LDH, SGOT, SGPT, alkaline phosphatase, glutamic dehydrogenase, RNAase; death a few hours after ingestion.
Martin, et al. (1969)	57-year-old man	40 ml		Somnolence; vomiting; sinus tachycardia ventricular extrasystoles; dyspnea; loss of blood pressure; cardiac arrest; death 24 hours after ingestion.
Schonborn, et al. (1970)	18-year-old man	50 ml	1 hour	Somnolent; cyanotic; diarrhea; 5.5 hours later shock of circulatory system; death after 17 hours in irreversible shock.
Yodaiken and Babcock (1973)	14-year-old boy	15 ml	2 hours	Headache; staggering; lethargy; periodic vomiting; blood pressure drop; cardiac arrest; pulmonary edema; refractory hypotension; death on 6th day.

platelet count were observed; fibrinolysis was increased up to four times its normal value. Martin, et al. (1969) reported a "thrombin time" after fibrinogen substitution of 59 seconds as contrasted to the normal 12 seconds. Post mortem examinations usually revealed thrombi in the pulmonary arterioles and capillaries, hemorrhages into the mucosa of the esophagus, stump of the stomach, rectum, and myocardial tissues.

Patients suffering from acute 1,2-dichloroethane poisoning developed diffuse dystrophic changes in brain and spinal cord cells which were qualified clinically as toxic encephalomyelopathy (Akimov, et al. 1978). One man who survived acute poisoning suffered irreversible mental defects, acute liver dystrophy, nephropathy, and anemia (Dorndorf, et al. 1976). Acute poisoning also caused an elevation of leukocytes in the blood and protein in the urine (Bonitenko, et al. 1977).

The effects of acute inhalation exposures to 1,2-dichloroethane are similar to those observed after ingestion, with death being attributed to respiratory and circulatory failure. (Wendel, 1948; Wirtschafter and Schwartz, 1939; Troisi and Cavallazzi, 1961). Nonfatal acute exposures have also been reported (Wirtschafter and Schwartz, 1939; McNally and Fostvedt, 1941). In a 1947 report, Rosenbaum reported that acute poisonings developed rapidly with repeated exposure of workers to concentrations of 75 to 125 ppm. Many persons exposed to lower concentrations of 1,2-dichloroethane reported delayed effects with the most severe reactions occurring after the evening meal (Byers, 1943).

Summaries of the acute effects of human exposures to 1,2-dichloroethane are similar for all routes of entry: ingestion, inhalation, and skin absorption. Such exposures result in nausea, vomiting, dizziness, internal bleeding, cyanosis, rapid but weak pulse, and unconsciousness. Acute exposures often lead to death from respiratory and circulatory failure. Chronic exposures to 1,2-dichloroethane have resulted in neurologic changes, loss of appetite and other gastrointestinal problems, irritation of mucous membranes, liver and kidney impairment, and in some cases, death (Natl. Inst. Occup. Safety Health, 1978a).

The anesthetic properties of 1,1,1-trichloroethane have been demonstrated in rats (Torkelson, et al. 1958), mice (Gehring, 1968), and dogs and monkeys (Krantz, et al. 1959). Based on minimum concentrations causing prostration in two hours, Lazarew (1929) determined that the 1,1,2-isomer was four times more toxic than the 1,1,1-isomer (Table 13).

TABLE 13

Effects of Trichloroethane Isomers on Mice

Isomer	Minimum Concentration for Response within 2 Hours of Exposure (mg/l)		
	proneness	loss of reflexes	death
1,1,1-	40	45	65
1,1,2-	10	15	60

Source: Lazarew, 1929

Adams, et al. (1950) determined an LC50 for rats exposed up to seven hours by inhalation to 1,1,1-trichloroethane (contained up to one percent 1,1-dichloroethane). At 18,000 ppm, half of the animals were dead in three hours (2.1 to 4.2 hours, 95 percent confidence limits); at 14,250 ppm half the animals were dead in seven hours (12,950 to 15,675 ppm, 95 percent confidence limits).

Both commercial grade and 1,1,1-trichloroethane (no inhibitors) were administered orally to rats, mice, rabbits, and guinea pigs for determination of an LD50 for each species (Torkelson, et al. 1958). Single doses of undiluted solvent were given by gavage (Table 14). No differences were observed in toxic responses of animals to solvents of varying purity.

During 1,1,1-trichloroethane anesthesia of dogs, two of the animals died suddenly (Rennick, et al. 1949). Further inhalation experiments indicated that at 0.33 to 0.53 g/kg, the solvent sensitized the heart to epinephrine-induced ventricular extrasystoles and ventricular tachycardia. Cardiac sensitization, an increased susceptibility of the heart to catecholamines, is induced by a number of halogenated hydrocarbons (Reinhardt, et al. 1973).

Electrocardiogram changes in three dogs were observed after an abrupt drop in blood pressure induced by 1,1,1-tricholoroethane anesthesia (Griffiths, et al. 1972). Dogs were sedated with sodium pentobarbital (20 mg/kg) before administration of about 125,000 ppm 1,1,1-trichloroethane. Krantz, et al. (1959) noted a drop in blood pressure to about one-half of its normal value prior to respiratory failure in 11 dogs and 10 monkeys administered 0.60 ml/kg

TABLE 14

LD50 After Oral Administration of
1,1,1-Trichloroethane in Laboratory Animals[a]

Characteristics of 1,1,1-Trichloroethane	Animal Sex/Species	LD50 (g/kg) Mean	95% Confidence Limits
2.4-3.0% dioxane	35 male rats	12.3	11.0-13.7
0.12-0.3% butanol	35 female rats	10.3	8.3-12.8
Trace of 1,2-dichloroethane	16 female mice	11.2	---
"	16 female rabbits	5.7	3.5-9.4
"	16 male guinea pigs	9.5	3.5- .3
Uninhibited	40 male rats	14.3	12.1-17.0
Not further defined	50 female rats	11.0	9.5-13.0
"	40 female mice	9.7	---
"	40 female rabbits	10.5	9.7-11.3
"	30 male guinea pigs	8.6	6.1-12.2

[a]Administered undiluted by gavage

Source: Torkelson, et al. 1958

and 0.59 ml/kg, respectively. EKG abnormalities were also noted.

Recent studies have demonstrated a relationship between changes in cardiovascular parameters and exposure to 1,1,1-trichloroethane including the following: Herd, et al. (1974) observed in dogs a dose-dependent two-phase drop in blood pressure and decreased peripheral resistance following an inhalation exposure; also in dogs, Reinhardt, et al. (1973) found 27.8 mg/l to be the minimal concentration causing sensitization of the heart to epinephrine-induced arrhythmias; Clark and Tinston (1973) reported the effective concentration for sensitization to be 40.7 mg/l in another group of dogs; in mice, Aviado and Belej (1974) noted arrhythmias during inhalation of 40 percent (v/v) 1,1,1-trichloroethane.

In summary, inhalation of 1,1,1-trichloroethane by various species of animals induces toxic effects in the central nervous, cardiovascular, and pulmonary systems, and in the liver and kidney (Truhaut, et al. 1973; Horiguchi and Horiguchi, 1971; Tsapko and Rappoport, 1972; Belej, et al. 1974; Herd, et al. 1974; Torkelson, et al. 1958; MacEwen and Vernot, 1974). In most animal studies, high concentrations were used. In the experiments cited, the lowest concentration producing toxic effects was 73 ppm, four hours per day from 50 to 120 days (Tsapko and Rappoport, 1972).

The effects most often reported following 1,1,1-tricholorethane exposure of humans are central nervous system disorders. These include changes in reaction time, perceptual speed, manual dexterity, and equilibrium; however, cardiovascular effects have not been observed at the concentrations

used in human exposures. Inhalation exposures of 450 ppm for eight hours caused eye, nose, and throat irritation, and decreased perceptive capabilities under stress conditions (Salvini, et al. 1971). Perceptual speed, reaction times, and manual dexterity were impaired in volunteers inhaling 350 ppm for three hours; impairment was not evident following inhalation of 250 ppm for two hours (Gamberale and Hultengren 1973). Two of 11 men inhaling 500 ppm 1,1,1-trichloroethane for 6.5 to 7 hours/day for five days responded with an abnormal modified Romberg's test (Stewart, et al. 1961).

An epidemiologic study of 151 matched pairs of employees was conducted in two adjacent textile plants, one of which used inhibited 1,1,1-trichloroethane as a general cleaning solvent (Kramer, et al. 1976). Employees in the study population had exposures to the solvent for six years or less at varying concentrations measured by breathing zone sampling and personal monitoring (eight hour time-weighted average, personal sampling concentrations ranged from 4 ppm to 217 ppm). Cardiovascular and hepatic observations were of primary interest. Statistical analysis of the data did not reveal any clinically pertinent findings which were associated with exposure to 1,1,1-trichloroethane.

LD50 concentrations of 1,1,2-trichloroethane (0.35 ml/kg in mice and 0.45 ml/kg in dogs, i.p.) caused kidney necrosis (Klaassen and Plaa, 1967). The effective dose for 50 percent of the animals (ED50) for kidney necrosis was 0.17 ml/kg in mice and 0.4 ml/kg in dogs 24 hours after receiving the compound. Forty-eight hours after receiving an ED50 dose based on serum glutamic-pyruvic transaminase

(SGPT) elevation (0.35 ml/kg, i.p.), the livers of treated dogs exhibited centrolobular necrosis.

Acute exposures of mice by inhalation to vapors of 1,1,2-trichloroethane (3750 ppm for 30 minutes) produced a significant elevation in SGPT measured 24 hours post exposure (Gehring, 1968). In comparison to the hepatotoxins carbon tetrachloride and chloroform, 1,1,2-trichloroethane was judged a moderate hepatotoxin as indicated by SGPT activity.

Twenty-four hours after the administration of a subacute oral dose of 1,1,1,2-tetrachloroethane to rabbits (0.5 g/kg body weight), the activity of enzymes indicating hepatoxicity was enhanced (Truhaut, et al. 1973). SGPT, serum glutamic oxaloacetic transaminase (SGOT), lactate dehydrogenase, and -hydroxy-butyrate dehydrogenase activities remained enhanced 72 hours after poisoning. Blood cholesterol and total lipid levels were also increased.

Acute exposures by inhalation to vapors of 1,1,2,2-tetrachloroethane produced anesthesia, death, fatty degeneration of the liver, and tissue congestion in mice (Muller, 1932; Horiguchi, et al. 1962) and rats (Horiguchi, et al. 1962). Exposure concentrations ranged from 5,900 ppm (three hours) to 11,400 ppm (six hours, two days). In monkeys exposed to 1,000 ppm or 4,000 ppm, two hours/day for 190 days, marked vacuolation of the liver was observed (Horiguchi, et al. 1962). A single four-hour exposure of rats to 1,000 ppm caused the death of three of six animals in 14 days (Smyth, et al. 1969). A three-hour exposure of mice to 600 ppm increased hepatic triglycerides and total lipids and decreased hepatic energy stores (Tomokuni, 1969).

Intravenous (i.v.) or intraperitoneal (i.p.) injection in guinea pigs of 1,1,2,2-tetrachloroethane (total of 0.7 ml in five doses in 14 days) caused weight loss, convulsions, death, and fatty degeneration of the liver and kidney (Muller, 1932). Two-tenths of a gram administered i.v. to rabbits was lethal in 30 hours (Muller, 1932). In mice, i.p. injection of 200 mg/kg was lethal in seven days (Natl. Res. Counc., 1952). Plaa and Larson (1965) reported death of nine of ten mice and increased urinary protein and glucose in the survivor resulting from the i.p. injection of 1.6 g/kg in corn oil on three alternate days.

Chronic exposures of rabbits by inhalation to 1,1,2,2-tetrachloroethane (14.6 ppm, four hours/day for 11 months) induced liver and kidney degeneration (Navrotskiy, et al. 1971). Inhalation by rats of 1.94 ppm, four hours/day up to 265 days, increased the number of white blood cells, pituitary adrenocorticotropic hormone, and the total fat content of the liver (Deguchi, 1972).

A number of human deaths have resulted from accidental or intentional 1,1,2,2-tetrachloroethane ingestion (Hepple, 1927; Elliot, 1933; Forbes, 1943; Lilliman, 1949; Lynch, 1967). In cases of occupational poisoning, effects of 1,1,2,2-tetrachloroethane have included dizziness, vomiting, malaise, headache, hand tremors, and abdominal pain (Lehmann and Schmidt-Kehl, 1936; Horiguchi, et al. 1962; Lobo-Mendonca, 1963; Wilcox, et al. 1915). Four deaths have been attributed to industrial exposure to 1,1,2,2-tetrachloroethane (Wilcox, et al. 1915).

Acute testing in laboratory animals indicated that hexachloroethane was moderately toxic when administered orally (Weeks, et al. 1979). The compound was dissolved in corn oil (50 percent, weight to volume) or methylcellolose (five percent, weight to volume) and administered by stomach tube to male and female rats and male guinea pigs. Following a 14-day observation period, the oral LD50 for male rats was 5,160 mg/kg in corn oil and 7,690 mg/kg in methylcellulose; in female rats, the oral LD50 was 4,460 and 7,080 mg/kg. In guinea pigs, the oral LD50 in corn oil was 4,970 mg/kg.

Daily oral doses (12 days) of hexachloroethane of 1,000 or 320 mg/kg administered to rabbits produced liver degeneration and toxic tubular nephrosis of the kidney. Animals were necropsied four days after the last exposure. Liver or kidney degeneration was not observed in rabbits receiving 100 mg/kg (Weeks, et al. 1979).

Exposure of dogs, guinea pigs, and rats by inhalation to 260 ppm hexachloroethane for six hours per day, five days/week for six weeks produced central nervous system toxicity in dogs and rats, and significantly higher liver-to-body weight ratios in guinea pigs and female rats. In male rats, the kidney-, spleen-, and testes-to-body ratios were significantly higher than controls. Half of the animals were sacrificed at the end of exposure and the remainder 12 weeks later. Evaluation of animals exposed to 48 ppm or 15 ppm revealed no adverse effects related to hexachloroethane exposure (Weeks, et al. 1979).

TABLE 15

Adverse Effects of Chloroethanes Reported in Animal Studies

Chemicals	Species	Adverse Effect
monochloroethane	unspecified	kidney damage; fatty changes in liver, kidney and heart
1,1-dichloro-ethane	cat	kidney damage
	dog	liver injury
	rat	liver injury; retarded fetal development
1,2-dichloro-ethane	bacterium	mutagen
	cat	retarded growth rate, fatty changes in liver; heart dilation; lung hyperemia
	dog	corneal clouding; fatty changes in liver; liver enlargement; weight loss
	fruit fly	mutagen
	guinea pig	fatty changes in liver; liver enlargement; weight loss
	monkey	fatty changes in liver
	rabbit	fatty changes in liver; hypotension; respiratory paralysis; EKG changes; anemia; bone marrow changes; liver dysfunction, hemorrhage and degeneration; kidney degeneration and dysfunction
	rat	embryotoxin; pulmonary congestion; fatty changes in liver
1,1,1,-trichloro-ethane	cat	neuromuscular reflex changes
	dog	sudden death; respiratory failure
	guinea pig	fatty changes in liver; lung irritation
	mouse	cardiac arrythmias; liver dysfunction; pulmonary congestion
	monkey	cardiac arrythmias; myocardial depression; respiratory failure; staggering gait; tachycardia; tremors
	rat	cardiac failure; pulmonary congestion; pneumonitis; staggering gait; weakness; semiconciousness; respiratory failure
1,1,2-trichloro-ethane	dog	liver and kidney injury
	guinea pig	liver and kidney injury
1,1,1,2-tetra-chloroethane	rabbit	embryotoxin
	rat	embryotoxin; liver dysfunction; mutagen
1,1,2,2-tetra-chloroethane	bacterium	mutagen
	dog	ascites; diarrhea; jaundice; liver enlargement; intestinal hemorrhage
	guinea pig	convulsions, weight loss; death
	monkey	anorexia; diarrhea; blood cell fluctuation; weight loss
	mouse	staggering gait; breathing difficulty; fatty degeneration of liver and kidney; death
	rabbit	altered immune system; altered blood chemistry; liver and kidney degeneration; fatty degeneration of liver and kidney; corneal reflex changes; liver enlargement; paralysis; death
	rat	blood cell changes; fatty degeneration of liver; liver dysfunction; death
pentachloro-ethane	cat	liver, kidney, and lung changes
	dog	fatty degeneration of liver; kidney and lung injury
	sheep	liver dysfunction
hexachloro-ethane	cattle	liver and kidney damage
	mouse	liver and kidney damage
	rat	liver and kidney damage
	sheep	liver and kidney damage

Source: National Institute for Occupational Safety and Health, 1978c.

TABLE 16

Summary of Human Toxicity, Chloroethanes

Chemical	System	Adverse Effect
monochloroethane	neurologic	central nervous system depression, headache, dizziness, incoordination feeling inebriated, unconsciousness
	gastrointestinal	abdominal cramps
	respiratory	respiratory tract irritation, respiratory failure
	cardiovascular	cardiac arrhythmias, cardiac arrest
	dermatological	skin irritation, frostbite, allergic eczema
	other	eye irritation, death
1,1-dichloroethane	neurologic	central nervous system depression
	respiratory	respiratory tract irritation
	dermatologic	skin burn
1,2-dichlorethane	neurologic	headache, dizziness, unconsciousness, vertigo, hand tremors, generalized weakness, sleepiness, nervousness, mental confusion
	hepatic	liver function abnormalities, cellular damage, toxic chemical hepatitis, jaundice, liver enlargement
1,1,1-trichloro-ethane	neurologic	central nervous system depression, headache, dizziness, incoordination, feeling inebriated, unconsciousness; impaired perceptual speed, manual dexterity and equilibrium; increased reaction time, lightheadeness, drowsiness, sleepiness, generalized weakness, ringing sound in ears, unsteady gait, burning and/or prickling sensation in hands and/or feet
	hepatic	cellular damage, liver function abnormalities
	gastrointestinal	nausea, vomiting, diarrhea
	cardiovascular	drop in blood pressure (hypotension), decrease in heart rate (bradycardia), cardiac arrhythmias
	hematologic	blood clotting changes
	dermatologic	dryness, cracking, scaliness, inflammation
	other	eye irritation, fatigue, death
1,1,2-trichloroethane		NIOSH is unaware of reports of adverse occupational exposure
1,1,1,2-tetrachloroethane		NIOSH is unaware of reports of adverse occupational exposure

TABLE 16 (continued)

Chemical	System	Adverse Effect
1,1,2,2-tetrachloroethane	neurologic	central nervous system depression, headache, feeling inebriated, unconsciousness, drowsiness, unsteady gait, vertigo, hand tremors, numbness in limbs, prickling sensation of fingers and toes, pain in soles of feet, loss of knee jerk, paralysis of some muscles of the hands and feet, inflammation of the peripheral nerves, slight paralysis of the soft palate, loss of the gag reflex, irritability, mental confusion, delirium, convulsions, stupor, coma
	hepatic	liver function abnormalitits, massive cell damage, toxic chemical hepatitis, jaundice, liver enlargement, sensation of pressure in the liver area
	gastrointestional	abdominal pain, nausea, vomiting, unpleasant taste in the mouth, loss of appetite (anorexia), vomiting of blood (hematemesis), increased flatulence, diarrhea, constipation, pale stools
	urologic	kidney damage, presence of bile pigments, albumen, and casts in the urine
	respiratory	excessive fluid in the lungs (pulmonary edema), respiratory paralysis
	cardiovascular	fatty degeneration of the heart muscle
	hematologic	anemia, increase in white blood cells, (and blood platelets)
	dermatologic	dryness,cracking, scaliness, inflamation, purpuric rash
	other	insomnia, general malaise, fatigue, excessive sweating, weight loss
pentachloroethane		NIOSH is unaware of reports of adverse occupational exposure
hexachloroethane	neurologic	inability to close eyelid; eye irritation, tearing of eyes, inflammation of delicate membrane lining the eye, visual intolerance to light, (photophobia)

Source: National Institute for Occupational Safety and Health, 1978c.

Laboratory animals (Table 15) and humans (Table 16) exposed to chloroethanes show similar symptoms of toxicity including eye and skin irritations, liver, kidney, and heart degeneration, and central nervous system depression.

Based on data derived from animal studies, the relative toxicity of chloroethanes is: 1,2-dichloroethane > 1,1,2,2-tetrachloroethane > 1,1,2-trichloroethane > hexachloroethane > 1,1-dichloroethane > 1,1,1-trichloroethane > monochloroethane. Available data are not sufficient to judge the relative toxicity of 1,1,1,2-tetrachloroethane or pentachloroethane.

Synergism and/or Antagonism

Pretreatment of mice with acetone or isopropyl alcohol (2.5 ml/kg, by gavage) enhanced the effects of threshold doses of 1,1,2-trichloroethane to produce an increased hepatotoxic response as measured by an increase in SGPT activity (Traiger and Plaa, 1974). Eighteen hours after pretreatment, the chlorinated hydrocarbon in corn oil was administered i.p.; 24 hours later, blood samples were taken by cardiac puncture. SGPT activity was not enhanced by 0.1 mg/kg 1,1,2-trichloroethane alone, but administered after acetone or isopropyl pretreatment, SGPT activity was significantly increased. The hepatotoxicity of 1,1,1-trichloroethane was not altered by pretreatment with acetone or isopropyl alcohol in these experiments.

Pretreatment of mice for three days with ethanol (5 g/kg, by gavage) enhanced 1,1,1-trichloroethane-induced sulfobromophthalein (BSP) retention, an indicator of liver dysfunction (Klaassen and Plaa, 1966). The chlorinated hydrocarbon administered on day four (2.75 ml/kg, i.p.)

increased BSP retention from 0.91 to 3.76 mg/100 ml. The effect of 1,1,2-trichloroethane on BSP retention was not potentiated by prior ingestion of ethanol. Cornish and Adefuin (1966) pretreated rats with ethanol which altered 1,1,1-trichloroethane hepatotoxicity as judged by SGOT activity. Pretreatment of rats with phenobarbital (i.p.) did not alter the effect of 1,1,1-trichloroethane on SGOT activity (Cornish, et al. 1973).

Exposure of rats to 3,000 ppm 1,1,1-trichloroethane for 24 hours decreased drug-induced sleeping time following the i.p. administration 24 hours post-exposure of hexobarbital, meprobamate, or zoxazolamine. Inhibitors of protein synthesis blocked the effect of 1,1,1-trichloroethane on hexobarbital-induced sleeping time (Fuller, et al. 1970). The concept that hepatic microsomal enzymes were induced was supported by in vitro stimulation of microsomal aniline hydroxylase activity by 1,1,1-trichloroethane (Van Dyke and Rikans, 1970).

Potentiation of toxicity was not observed in extensive studies with a mixture (by weight) of 1,1,1-trichloroethane (75 percent) and tetrachloroethylene (25 percent) in mice, rats, guinea pigs, rabbits, dogs, and human subjects (Rowe, et al. 1963).

Teratogenicity

No literature was found concerning the teratogenic effects of monochloroethane, 1,1,2-trichloroethane, 1,1,1,2-tetrachloroethane, 1,1,2,2-tetrachloroethane or pentachloroethane.

Inhalation of 1,1-dichloroethane (3,800 or 6,000 ppm) by pregnant rats seven hours per day on days 6 through 15

of gestation had no effect on the incidence of fetal resorptions, on fetal body measurements, or on the incidence of gross or soft tissue anomalies. A significantly increased incidence of delayed ossification of sternebrae was associated with exposure to 6,000 ppm 1,1-dichloroethane which reflects retarded fetal development rather than a teratological effect (Schwetz, et al. 1974).

After a six-month exposure of female rats by inhalation of 1,2-dichloroethane (57 mg/m^3, four hours/day, six days/week), animals were bred and exposed throughout gestation. Litter size, the number of live births, and fetal weights were reduced (Table 17). Tissue and skeletal anomalies were not reported (Vozovaya, 1974).

TABLE 17
Effect of 1,2-Dichloroethane
on Fetal Rat Development

Treatment	Litter Size	Percent Live Fetuses	Fetal Weight(g)
Filtered Air	9.7	94.9	6.44
1,2-dichloroethane[a]	6.5	76.9	5.06

[a] 57 mg/m^3, 4 hrs/day, 6 days/week, throughout gestation

Source: Vozovaya, 1974

Twenty-three pregnant Sprague-Dawley rats and 13 Swiss-Webster mice inhaled 875 ppm 1,1,1-trichloroethane seven hours a day, from days 6 through 15 of gestation. There was no effect on the average number of implantation sites per litter, litter size, the incidence of fetal resorptions, fetal sex ratios, or fetal body measurements among mice

or rats (Dunnett test $p < 0.05$). Soft tissue and skeletal anomalies occurred in 1,1,1-trichloroethane-exposed animals which did not occur in control animals; however, the incidences were not statistically significant (Fisher Exact probability test, $p < 0.05$) (Schwetz, et al. 1975).

Pregnant Sprague-Dawley rats were treated from day 6 through day 16 of gestation with hexachloroethane administered either by inhalation (15, 48 or 260 ppm, 6 hours/day) or by stomach tube (50, 100 or 500 mg/kg/day). Dams receiving 500 mg/kg/day orally had a significantly lower number of live fetuses per litter and higher fetal resorption rates. Fetal parameters in all other groups were within normal limits. No significant skeletal or soft tissue anomalies resulted from hexachloroethane exposures (Weeks, et al. 1979).

Mutagenicity

No data were found in the literature regarding the mutagenic potential of mono -; 1,1-di -; 1,1,1-tri -; 1,1,2-tri -; 1,1,1,2-tetra -; or penta - chloroethane.

1,2-Dichloroethane and 1,1,2,2-tetrachloroethane were moderately mutagenic in the Ames Salmonella assay for strains TA 1530 and TA 1535, and for the E. coli DNA polymerase-deficient system (Brem, et al. 1974). Rosenkranz (1977) determined the order of mutagenic activity toward S. typhimurium and E. coli to be 1,1,2,2-tetrachloroethane > 1,2-dichloroethane. Mutagenicity of 1,2-dichloroethane was not dependent on NADPH (Rannug and Ramel, 1977) or microsomes (Rannug, et al. 1978) but metabolic activation was accomplished by a factor in the soluble fraction (115,000 x g supernatant).

A conjugation product, S-chloroethyl cysteine, proved to be more mutagenic than the parent compound (Rannug, et al. 197c).

Metabolites of 1,2-dichloroethane varied in their mutagenic activity for Salmonella strains: 2-chloroacetaldehyde was mutagenic for strain TA100 (McCann, et al. 1975) and strains TA1530 and TA1535 (Rannug, et al. 1978); 2-chloroethanol was less mutagenic and 2-chloroacetic acid was inactive (McCann, et al. 1975).

1,2-Dichloroethane induced highly significant increases in somatic mutation frequencies in Drosophila melanogaster (Nylander, et al. 1978). Morphological and chlorophyll mutations in eight varieties of peas were induced by treatment of seeds with 1,2-dichloroethane (Kirichek, 1974).

Hexachloroethane was not mutagenic for five strains of Salmonella or yeast (Saccharomyces cerevisiae D4) in the absence or presence of induced rat liver S-9 preparations (Weeks, et al. 1979).

Carcinogenicity

1,2-Dichloroethane: A bioassay of 1,2-dichloroethane for carcinogenic potential was conducted by the National Cancer Institute (1978a). Technical grade 1,2-dichloroethane (impurities less than ten percent) in corn oil was administered by stomach tube to 50 male and 50 female animals of each test species (Osborne-Mendel rats and B6C3F1 mice) at two dosage levels, five days/week. Mice received continuous treatments for 78 weeks. Rats received continuous treatments for 35 weeks; from week 36 through week 78, periods of one week of no treatment were alternated with periods of four

weeks of treatment. Dosage levels were manipulated during the experiment: the two initial dose levels for male and female rats were 100 and 50 mg/kg/day; doses were increased to 150 and 75 mg/kg/day, then decreased to initial levels. The high time-weighted average dose for rats was 95 mg/kg/day; the low time-weighted average dose was 47 mg/kg/day. Male mice received initial high doses of 150 mg/kg/day and low doses of 75 mg/kg/day. These doses were raised to 200 and 100 mg/kg/day. The high time-weighted average dose was 195 mg/kg/day; the low was 97 mg/kg/day. Female mice received initial high doses of 250 mg/kg/day and low doses of 125 mg/kg/day. These doses were raised to 400 and 200 mg/kg/day, then decreased to 300 and 150 mg/kg/day. The high time-weighted average dose was 299 mg/kg/day; the low 149 mg/kg/day. After 78 weeks of treatment, rats were observed either until death or for an additional 32 weeks; mice were observed an additional 12 or 13 weeks (Natl. Cancer Inst., 1978a).

Control groups consisted of 20 male and 20 female animals of each test species. Vehicle controls were treated with corn oil by stomach tube according to the treatment regimen of the test animals. Untreated controls were not intubated.

Treatment of rats and mice with 1,2-dichloroethane induced a number of benign and malignant neoplasms (Table 18).

The incidences of squamous cell carcinomas of the forestomach, subcutaneous fibromas, and hemangiosarcoma in male rats and the incidence of mammary adenocarcinomas in female rats were significantly correlated with increased doses of 1,2-dichloroethane according to the Fisher exact test and the Cochran-Armitage test (Table 19).

TABLE 18

Summary of Incidence of Neoplasms in Rats and Mice Ingesting 1,2-Dichloroethane for 78 Weeks

Species	Sex	Dose	Total Number of Animals with Tumors		
			Benign	Malignant	Metastases
Rat	male	untreated	2	6	-
		corn oil	3	1	-
		47	7	15	1
		95	17	16	4
	female	untreated	12	6	1
		corn oil	7	-	-
		47	20	8	-
		95	18	25	2
Mouse[b]	male	untreated	-	2	-
		corn oil	-	4	1
		97	1	15	1
		195	15	22	1
	female	untreated	1	3	-
		corn oil	1	5	-
		149	12	26	6
		299	16	21	6

[a]Compound administered in corn oil by stomach tube five days/week. Concentration is a time-weighted average expressed in mg/kg/day.

[b]Two control groups: 20 animals per group. Experimental groups: 50 animals at each dosage level.

Source: National Cancer Institute, 1978a.

TABLE 19

Percent[a] of Rats with 1,2-Dichloroethane Induced Neoplasms[b]

Tumor Type	Male[c]		Female[c]	
	Low dose[d]	High dose[e]	Low dose[d]	High dose[e]
Squamous-cell carcinoma: stomach	6	18	--	--
Hemangiosarcoma: all sites	22	16	--	--
Fibroma: subcutaneous	10	12	--	--
Adenocarcinoma: mammary gland	--	--	2	36

[a]Percent: animals with tumors/animals examined x 100

[b]Includes only neoplasms that were statistically correlated with 1,2-dichloroethane treatment

[c]Experimental groups: 50 animals at each dosage level
Two control groups: 20 animals per group-receiving corn oil or no treatment

[d]The low time-weighted average dose: 47 mg/kg/day

[e]The high time-weighted average dose: 95 mg/kg/day

Source: National Cancer Institute, 1978a.

In male and female mice treated with 1,2-dichloroethane, the incidence of alveolar/bronchiolar adenomas was statistically significant. The incidence of mammary adenocarcinomas and of endometrial tumors in female mice and the incidence of hepatocellular carcinomas in male mice were statistically positively correlated with treatment (Table 20; Natl. Cancer Inst., 1978a).

1,1,1-Trichloroethane: The National Cancer Institute (1977) conducted a bioassay of 1,1,1-trichloroethane to determine potential carcinogenicity. Technical grade 1,1,1-trichloroethane (impurities: three percent p-dioxane, two percent unidentified) in corn oil was administered by stomach tube to 50 male and 50 female animals of each test species (Osborne-Mendel rats and B6C3F1 mice) at two dosage levels, five days/week for 78 weeks. During the experiment, doses for mice were increased from 4,000 and 2,000 mg/kg/day to 6,000 and 3,000 mg/kg/day. The high time-weighted average dose was 5,615 mg/kg/day; the low was 2,807 mg/kg/day. Doses for rats remained constant at 1,500 and 750 mg/kg/day. All surviving rats were killed at 117 weeks of age; surviving mice were killed at 95 weeks (Natl. Cancer Inst., 1977).

Control groups consisted of 20 animals of each sex and species. Carbon tetrachloride was administered as the positive control.

TABLE 20

Percent[a] of Mice with 1,2-Dichloroethane Induced Neoplasms[b]

Tumor Type	Male[c]		Female[c]	
	Low dose[d]	High dose[e]	Low dose[f]	High dose[g]
Alveolar/bronchiolar-adenoma	2	31	14	31
Endometrial sarcoma	--	--	4	6
Hepatocellular carcinoma	13	25	--	--

[a]Percent: animals with tumors/animals examined x 100

[b]Includes only neoplasms that were statistically correlated with 1,2-dichloroethane treatment

[c]Experimental groups: 50 animals at each dosage level
Two control groups: 20 animals per group-receiving corn oil or no treatment

[d]The low time-weighted average dose: 97 mg/kg/day

[e]The high time-weighted average dose: 195 mg/kg/day

[f]The low time-weighted average dose: 149 mg/kg/day

[g]The high time-weighted average dose: 299 mg/kg/day

Source: National Cancer Institute, 1978a.

There was a moderate depression of body weight in male and female rats and mice throughout the study. Male and female rats given 1,1,1-trichloroethane exhibited earlier mortality than the untreated controls. The statistical test for the dose-related trend was significant ($P < 0.04$). Survival of mice was significantly decreased; in female mice there was a dose-related trend in the numbers surviving ($P=0.002$). Fewer rats receiving 1,1,1-trichloroethane survived at both 78 and 110 weeks than did positive control rats receiving carbon tetrachloride, a known carcinogen (Table 21). Chronic murine pneumonia was the most probable cause for the high incidence of deaths in several groups.

Although a variety of neoplasms was observed in both 1,1,1,-trichloroethane-treated and matched-control rats and mice (Table 22), no relationship was established between dosage groups, species, sex, type of neoplasm, or site of occurrence. The shortened life-spans of the rats and mice made an assessment of ingested 1,1,1-trichloroethane carcinogenicity impossible (Natl. Cancer Inst., 1977). The National Cancer Institute is currently retesting the compound.

Price, et al. (1978) demonstrated the <u>in vitro</u> transforming potential of 1,1,1-trichloroethane (99.9 percent pure) using the Fischer rat embryo cell system (F1706). Rat embryo cell cultures were treated with 1,1,1-trichloroethane, diluted in growth medium, for 48 hours. After nine subcultures, the transformed cells (characterized by morphology and formation of macroscopic foci in semi-soft agar) were inoculated into newborn Fischer rats. By 68 days, the transformed

TABLE 21

Comparison of Survival of Control Groups,
1,1,1-Trichloroethane-Treated and
Carbon Tetrachloride-Treated (Positive Control) Rats

Group	1,1,1-Trichloroethane			Carbon Tetrachloride		
	Initital No. of Animals	Number Alive at 78 weeks	Number Alive at 110 weeks	Initial No. of Animals	Number Alive at 78 weeks	Number Alive at 110 weeks
MALE						
Control	20	7	0	20	20	12
Low Dose	50	1	0	50	34	15
High Dose	50	4	0	50	35	8
FEMALE						
Control	20	14	3	20	18	14
Low Dose	50	9	2	50	38	20
High Dose	50	12	1	50	21	14

Source: National Cancer Institute, 1977.

TABLE 22

Summary of Neo[illegible]ns in Rats and Mice Ingesting
1,1,1-Trichloroethane for 78 Weeks

Species	Sex	Number of Animals	Dose[a]	Total Number of Tumors	Number of Tumors Observed						
					Liver, Spleen	Lung	Kidney, Bladder	Skin	Heart, Vasculature	Brain, Pituitary	Other
Rat	Male	20	-	3	1	-	-	1	-	-	1
		50	750	6	1	-	-	-	1	1	3
		50	1500	4	-	-	1	-	1	-	3
	Female	20	-	14	-	-	-	-	-	3	11
		50	750	6	-	-	-	-	-	2	4
		50	1500	12	1	-	-	1	1	1	8
Mouse	Male	20	-	5	2	1	-	-	-	-	2
		50	2807	2	1	1	-	-	-	-	-
		50	5615	9	8	1	-	-	-	-	-
	Female	20	-	5	2	-	2	-	-	1	5
		50	2807	2	1	-	-	1	-	-	-
		50	5615	3	-	1	-	1	-	-	1

[a]Compound administered in corn oil by stomach tube five days per/week.
Concentration is a time-weighted average expressed in mg/kg/day.

Source: National Cancer Institute, 1977.

cells had grown as undifferentiated fibrosarcomas at the inoculation sites in all tested animals. Acetone, the negative control, did not induce tumors by 82 days after inoculation (Price, et al. 1978).

1,1,2-Trichloroethane: A bioassay of 1,1,2-trichloroethane for possible carcinogenicity was conducted by the Natl. Cancer Inst. (1978b). Technical grade 1,1,2-trichloroethane (92.7 percent pure) in corn oil was administered by stomach tube to 50 male and 50 female animals of each test species (Osborne-Mendel rats and B6C3F1 mice) at two dosage levels, five days/week for 78 weeks. During the experiment, doses for rats were increased from 70 and 30 mg/kg/day to 100 and 50 mg/kg/day. The high time-weighted average dose was 92 mg/kg/day; the low was 46 mg/kg/day. Doses for mice were increased from 300 and 150 mg/kg/day to 400 and 200 mg/kg/day. The high time-weighted average dose was 390 mg/kg/day; the low 195 mg/kg/day. After 78 weeks of treatment, rats were observed an additional 35 weeks; mice observed for an additional 13 weeks (Natl. Cancer Inst., 1978b).

Control groups consisted of 20 animals of each sex and species. Vehicle controls were treated with corn oil by stomach tube at the same rate as the high dose group of the same sex; untreated control animals were not intubated.

Adrenal cortical carcinomas, transitional-cell carcinoma of the kidney, renal tubule adenoma, and hemangiosarcomas of the spleen, pancreas, abdomen, and subcutaneous tissue were some of the neoplasms observed in treated, but not control rats. Because a statistically significant difference could not be found between the test group and the controls,

carcinogenicity of 1,1,2-trichloroethane in Osborne-Mendel rats cannot be inferred (Table 23; Natl. Cancer Inst., 1978b).

On the other hand, treatment of mice with 1,1,2-trichloroethane was correlated with an increased incidence of hepatocellular carcinoma (Table 24). Both the Fisher exact test comparing tumor incidences of dosed to control groups and the Cochran-Armitage test for positive dose-related trend established that this correlation was significant (P 0.001). The Cochran-Armitage test also showed a significant dose-related association between 1,1,2-trichloroethane treatment and incidence of pheochromocytoma of the adrenal gland in male and female mice. Fisher exact tests, however, confirmed this association only for high dose female mice, not other mouse groups (Natl. Cancer Inst., 1978b).

1,1,2,2-Tetrachloroethane: Technical grade 1,1,2,2-tetrachloroethane (90 percent pure) in corn oil was administered by stomach tube to 50 male and 50 female animals of each test species (Osborne-Mendel rats and B6C3F1 mice) at two dosage levels, five days/week. Mice received continuous treatments for 78 weeks. Rats received continuous treatment for 32 weeks; from week 33 through week 78, periods of one week of no treatment were alternated with periods of four weeks of treatment. Dosage levels were manipulated during the experiment: the initial dosages for male and female rats were 100 mg/kg/day and 50 mg/kg/day; dosage levels for males were increased to 130 mg/kg/day and 65 mg/kg/day. The high time-weighted average dose for male rats was 108 mg/kg/day; the low was 62 mg/kg/day. For female rats, the high time-weighted average dose was 76 mg/kg/day and the

TABLE 23

Summary of Incidence of Neoplasms in Rats and Mice Ingesting 1,1,2-Trichloroethane for 78 Weeks

Species	Sex	Dose[a]	Total Number of Animals with Tumors		
			Benign	Malignant	Metastases
Rat[b]	Male	Untreated	1	3	1
		Corn Oil	3	5	-
		46	11	12	1
		92	4	8	-
	Female	Untreated	9	3	-
		Corn Oil	4	-	-
		46	29	6	-
		92	15	9	2
Mouse[b]	Male	Untreated	2	3	-
		Corn Oil	1	5	-
		195	6	27	-
		390	9	38	3
	Female	Untreated	1	3	-
		Corn Oil	-	4	-
		195	4	18	-
		390	16	40	3

[a]Compound administered in corn oil by stomach tube five days/week. Concentration is a time-weighted average expressed in mg/kg/day.

[b]Two control groups: 20 animals per group
Experimental groups: 50 animals per dosage level.

Source: National Cancer Institute, 1978b.

TABLE 24

Incidence of Hepatocellular Carcinoma In Mice Ingesting 1,1,2-Trichloroethane for 78 Weeks

Sex	Dose[a]	Number of Animals Examined	Hepatocellular Carcinoma No. of Animals	Hepatocellular Carcinoma Percent
Male[b]	Untreated	17	2	12
	Corn Oil	20	2	10
	195	49	18	37
	390	49	37	76
Female[b]	Untreated	20	2	10
	Corn Oil	20	0	--
	195	48	16	33
	390	45	40	89

[a]Compound administered in corn oil by stomach tube five days/week. Concentration is a time-weighted average expressed in mg/kg/day.

[b]Two control groups: 20 animals per group.
Experimental groups. 50 animals per dosage level.

Source: National Cancer Institute, 1978b.

low was 43 mg/kg/day. The initial dose for male and female mice was 200 mg/kg/day. This high dose was first increased to 300 mg/kg/day, then to 400 mg/kg/day, and finally lowered to 300 mg/kg/day. The initial low dose for both sexes was 100 mg/kg/day. The low dose was increased to 150 mg/kg/day. The high time-weighted average dose for male and female mice was 282 mg/kg/day; the low was 142 mg/kg/day. After 78 weeks of treatment, rats were observed for an additional 32 weeks and mice an additional 12 weeks (Natl. Cancer Inst., 1978c).

Control groups consisted of 20 animals of each sex and species. Vehicle controls were treated with corn oil by stomach tube; untreated controls were not intubated.

The incidence of hepatocellular carcinoma in male and female mice was positively correlated ($P < 0.001$) with dosage level (Table 39). Although one neoplastic nodule and two hepatocellular carcinomas, rare tumors in the Osborne-Mendel rat, were seen in high dose male rats, the incidence of neoplasms in rats of either sex was not statistically significant (Table 25; Natl. Cancer Inst., 1978c).

Hexachloroethane: Technical grade hexachloroethane (98 percent pure) in corn oil was administered by stomach tube to 50 male and 50 female animals of each test species (Osborne-Mendel rats and B6C3F1 mice) at two dosage levels, five days/week. Mice received continuous treatments for 78 weeks. Rats received continuous treatments for 22 weeks; from week 23 through week 78, periods of one week of no treatment were alternated with periods of four weeks of treatment. Male and female rats received high doses of

TABLE 25

Incidence of Hepatocellular Carcinoma in Mice Ingesting 1,1,2,2-Tetrachloroethane[a] for 78 Weeks

Sex	Dose[b]	Number of Animals Examined	Hepatocellular Carcinoma	
			Number	Percent
Male[c]	Untreated	16	2	13
	Corn Oil	18	1	6
	142	50	13	26
	282	49	44	90
Female[c]	Untreated	18	0	--
	Corn Oil	20	0	--
	142	48	30	63
	282	47	43	91

[a]Incidence of hepatocellular carcinoma indicated a highly significant ($P < 0.001$) positive dose-related trend in mice of both sexes.

[b]Compound administered in corn oil by stomach tube five days/week. Concentration is a time-weighted average expressed in mg/kg/day.

[c]Two control groups: 20 animals per group.
Experimental groups: 50 animals per dosage level.

Source: National Cancer Institute, 1978c.

TABLE 26

Summary of Incidence of Neoplasms in Rats and Mice Ingesting 1,1,2,2-Tetrachloroethane for 78 Weeks

Species	Sex	Dose[a]	Total Number of Animals with Tumors		
			Benign	Malignant	Metastases
Rat[b]	Male	Untreated	2	6	-
		Corn Oil	9	6	-
		62	11	7	1
		108	13	9	-
	Female	Untreated	12	6	1
		Corn Oil	11	1	-
		43	24	7	1
		76	21	5	-
Mouse[b]	Male	Untreated	2	9	-
		Corn Oil	3	1	-
		142	3	17	1
		282	3	45	-
	Female	Untreated	1	1	-
		Corn Oil	-	1	1
		142	2	33	-
		282	2	43	-

[a]Compound administered in corn oil by stomach tube five days/week. Concentration is a time-weighted average expressed in mg/kg/day.

[b]Two control groups: 20 animals per group.
Experimental groups: 50 animals per dosage level.

Source: National Cancer Institute, 1978c.

500 mg/kg/day and low doses of 250 mg/kg/day. Although dosage levels remained constant throughout the study, treatment was not continuous: the high and low time-weighted average doses for rats were 432 and 212 mg/kg/day. Male and female mice received initial high doses of 1,000 mg/kg/day and low of 500 mg/kg/day. The doses were increased to 1,200 mg/kg/day and 600 mg/kg/day. The high time-weighted average dose was 1,179 mg/kg/day; the low time-weighted average dose 570 mg/kg/day (Natl. Cancer Inst., 1978d). After 78 weeks of treatment, rats were observed for an additional 33 or 34 weeks, mice an additional 12 or 13 weeks.

Control groups consisted of 20 animals of each sex and test species. Vehicle controls were treated with corn oil by stomach tube; untreated animals were not intubated.

Toxic tubular nephropathy was observed in all groups of treated animals: in rats, 18 to 66 percent, and in mice, [illegible] to 100 percent. Male and female rats exhibited increased mortality rates which were statistically correlated with increased dosage. This trend was not evident with mice of either sex (Natl. Cancer Inst., 1978d).

In mice of both sexes, the incidence of hepatocellular carcinoma was positively correlated ($P < 0.001$) with hexachloroethane treatment (Table 27). There was no evidence of hexachloroethane induced neoplasms in rats of either sex (Table 28; Natl. Cancer Inst., 1978d).

A summary of the results of the NCI bioassays of chloroethanes is presented in Table 29.

TABLE 27

Incidence of Hepatocellular Carcinoma in Mice Ingesting Hexachloroethane for 78 Weeks

Sex	Dose[a]	Number of Animals Examined	Hepatocellular Carcinoma	
			No. of Animals	Percent
Male[b]	Untreated	18	1	6
	Corn Oil	20	3	15
	590	50	15	30
	1179	49	31	63
Female[b]	Untreated	18	0	0
	Corn Oil	20	2	10
	590	50	20	40
	1179	49	15	31

[a]Compound administered in corn oil by stomach tube five days/week. Concentration is a time-weighted average expressed in mg/kg/day.

[b]Two control groups: 20 animals per group.
Experimental groups: 50 animals per dosage level.

Source: National Cancer Institute, 1978d.

TABLE 28

Summary of Incidence of Neoplasms in Rats and Mice[a]
Ingesting Hexachloroethane for 78 Weeks

Species	Sex	Dose[a]	Total Number of Animals with Tumors		
			Benign	Malignant	Metastases
Rat[b]	Male	Untreated	6	5	-
		Corn Oil	7	4	1
		212	12	6	2
		423	8	1	-
	Female	Untreated	11	6	1
		Corn Oil	11	4	1
		212	29	6	1
		423	18	3	1
Mouse[b]	Male	Untreated	0	3	1
		Corn Oil	1	3	-
		590	1	16	1
		1179	5	33	-
	Female	Untreated	3	2	1
		Corn Oil	2	6	-
		590	3	31	1
		1179	4	24	-

[a]Compound administered in corn oil by stomach tube five days/week. Concentration is a time-weighted average expressed in mg/kg/day.

[b]Two control groups: 20 animals per group.
Experimental groups: 50 animals per group.

Source: National Cancer Institute, 1978d.

An estimated five million workers are potentially exposed to one or more chloroethanes (Natl. Inst. Occup. Safety Health, 1978c). To date, no epidemiological relationship has been found between chloroethane exposure and human cancer.

CRITERION FORMULATION

Existing Guidelines and Standards

OSHA standards and NIOSH recommended standards are based on exposure by inhalation (Table 30). Based on information available in 1976b, the National Institute for Occupational Safety and Health recommended that occupational exposures to 1,2-dichloroethane not exceed 5 ppm (20 mg/m^3) determined as a time-weighted average for up to a 10-hour work day, 40-hour work week. Peak concentrations should not exceed 15 ppm (60 mg/m^3) as determined by a 15-minute sample. The current enforced OSHA exposure standard is 50 ppm, time-weighted average for up to a 10-hour work day, 40-hour work week. NIOSH (1976b) issued criteria for a recommended standard of 200 ppm for occupational exposures to 1,1,1-trichloroethane. This recommendation to change the standard from 350 ppm is based on central nervous system responses to acute exposures in man, cardiovascular and respiratory effects in man and animals, and the absence of reported effects in man at concentrations below the proposed limit.

Current Levels of Exposure

Estimates of human exposure to chloroethanes via ingestion are not available for the general population. NIOSH (1978c) estimated that of over five million workers exposed by inhalation and dermal routes to chloroethanes, 4.5 million are exposed to 1,2-dichloroethane or 1,1,1-trichloroethane (Table 31).

TABLE 30

Chloroethane Exposure Standards

Chemical	OSHA Exposure Standard (ppm)	NIOSH Recommended Exposure Standard (ppm)
monochloroethane	1,000	none
1,1-dichloroethane	100	none
1,2-dichloroethane	50	5
1,1,1-trichloroethane	350	200
1,1,2-trichloroethane	10	none
1,1,1,2-tetrachloroethane	none	none
1,1,2,2-tetrachloroethane	5	1
pentachloroethane	none	*
hexachloroethane	1	*

*NIOSH has tentative plans for a Criteria Document for a Recommended Standard for this substance

Source: National Institute for Occupational Safety and Health, 1978c.

TABLE 31

Chloroethane Exposures and Production

Chemical	Estimated number of workers exposed	Annual Production quantities (pounds)
monochloroethane	113,000	670 million (1976)
1,1-dichloroethane	4,600	b
1,2-dichloroethane	1,900,000	8 billion (1976)
1,1,1-trichloroethane	2,900,000	630 million (1976)
1,1,2-trichloroethane	112,000	c
1,1,1,2-tetrachloroethane	a	b
1,1,2,2-tetrachloroethane	11,000	c
pentachloroethane	a	b
hexachloroethane	1,500	b,d

[a]NIOSH estimates not available
[b]Does not appear to be commercially produced in the United States
[c]Direct production information not available
[d]730,000 kg were imported in 1976

Source: National Institute for Occupational Safety and Health, 1978c.

In the general population there are chronic exposures to variable amounts in air and finished water. Chloroethanes are present in many commercial products, and exposure of the population depends on the tendency of individuals to read and heed instructions.

Special Groups at Risk

Workers who are occupationally exposed to chloroethanes by inhalation and/or dermal absorption represent a special group at risk (Table 31). Epidemiological studies have not disclosed a relationship between exposure to chloroethanes and cancer; however, four chloroethanes have proved to be carcinogenic in at least one species of rodent (Natl. Cancer Inst., 1978a,b,c,d). Those individuals who are exposed to known hepatotoxins or have liver disease may constitute a group at risk.

Basis and Derivation of Criterion

TABLE 32

Criteria for Chloroethanes

Compound	Criterion	Reference
Monochloroethane	None	
1,1-Dichloroethane	None	
1,2-Dichloroethane	7.0 µg/l - Carcinogenicity data	NCI, 1978a
1,1,1-Trichloroethane	15.7 mg/l - mammalian toxicity data	NCI, 1977
1,1,2-Trichloroethane	2.7 µg/l - Carcinogenicity data	NCI, 1978b
1,1,1,2-Tetrachloroethane	None	
1,1,2,2-Tetrachloroethane	1.8 µg/l - Carcinogenicity data	NCI, 1978c
Pentachloroethane	None	
Hexachloroethane	5.9 µg/l - Carcinogenicity data	NCI, 1978d

At the present time, there is insufficient mammalian toxicological information to establish a water criterion for human health for the following chloroethanes: monochloroethane, 1,1-dichloroethane, 1,1,1,2-tetrachloroethane and pentachloroethane. Available evidence indicates that the general population is exposed to only trace levels of 1,1-dichloroethane, 1,1,1,2-tetrachloroethane and pentachloroethane. Although inhalation exposure to monochloroethane is more widespread, it is considered one of the least toxic of the chloroethanes. Should significant levels of exposure be documented in the future, it will be necessary to conduct more extensive toxicologic studies with these chloroethanes.

The criterion for 1,1,1-trichloroethane is based on the National Cancer Institute bioassay for possible carcinogenicity (1977). Results of the study showed that the survival of both Osborne-Mendel rats and B6C3F1 mice was significantly decreased in groups receiving oral doses of 1,1,1-trichloroethane. Chronic murine pneumonia may have been responsible for the high incidence of natural deaths. A variety of neoplasms was observed in both species, however, the incidence of specific malignancies was not significantly different from those observed in control animals. Survival time was significantly decreased in rats receiving the high dose, therefore, the criterion for 1,1,1-trichloroethane is based on the low dose in rats (750 mg/kg body weight, 5 days/week for 78 weeks) which produced toxic effects in a number of systems. It should be recognized that the actual no-observable-adverse-effect level (NOAEL) will be lower. However,

use of the lowest-minimal-effect dose as an estimate of an "acceptable daily intake" has been practiced by the National Academy of Sciences (1977). Thus, assuming a 70 kg body weight and using a safety factor of 1,000 (Natl. Acad. Sci., 1977) the following calculation can be derived:

$$\frac{750 \text{ mg/kg} \times 70 \text{ kg} \times 5/7 \text{ day}}{1000} = 37.5 \text{ mg/day}$$

Therefore, consumption of 2 liters of water daily and 18.7 grams of contaminated fish having a bioconcentration factor of 21, would result in, assuming 100 percent gastrointestinal absorption of 1,1,1-trichloroethane, a maximum permissible concentration of 15.7 mg/l for ingested water:

$$\frac{37.5 \text{ mg/day}}{2 \text{ liters} + (21 \times .0187) \times 1.0} = 15.7 \text{ mg/l}$$

Based on available literature, 1,1,2-tri-, 1,1,2,2-tetra-, and hexachloroethane are considered to be carcinogenic in at least one rodent species (Natl. Cancer Inst., 1978b,c,d). In the case of these three chloroethanes, a statistical evaluation of the incidences of hepatocellular carcinomas revealed a significant positive association between the administration of the respective chloroethanes and tumor incidence. It can be concluded that under the conditions of the NCI bioassay, 1,1,2-tri; 1,1,2,2-tetra-; and hexachloroethane are carcinogenic in B6C3F1 mice, inducing (in all cases) hepatocellular carcinomas in either male or female mice.

Estimated risk levels for these chloroethanes in water can be calculated using a linear, non-threshold model with the results from the NCI bioassays (see Appendix 1 for detailed assumptions and calculations). The model assumes a risk

of 1 in 100,000 of developing cancer as a result of drinking 2 liters of water per day containing chloroethane at the concentrations used in the bioassays. Allowances are also made for consuming fish from chloroethane contaminated waters. Based upon these assumptions, the following criteria can be calculated:

Chloroethane	Dose[a] (mg/kg)	Criteria (µg/l)
1,1,2-trichloroethane	279	2.7
1,1,2,2-tetrachloroethane	203	1.8
hexachloroethane	842	4.4

[a]Five days per week for 78 weeks

Under the conditions of an NCI bioassay (1978a), 1,2-dichloroethane is carcinogenic, inducing a statistically significant number of squamous cell carcinomas of the forestomach and hemangiosarcomas of the circulatory system in male rats, mammary adenocarcinomas in female rats and mice, and endometrial tumors in female mice. The criterion for 1,2-dichloroethane is based on the high dose (107 mg/kg/body weight, 5 days/week for 78 weeks) which induced mammary adenocarcinomas in female rats. Using a linear, non-threshold model and including the consumption of fish from chloroethane contaminated waters the criterion for 1,2-dichloroethane is 7.0 µg/l.

It must be recognized that the NCI studies were designed to provide a "yes/no" answer to the carcinogenicity of a chemical in rats and mice. In some cases, it is difficult to justify extrapolation of data from NCI studies in order to assess the risk to man of chronic exposure to low concen-

trations of a chemical. Those who assess risk should be aware of the following: impurities in technical grade chloroethanes were not identified; chloroethanes were administered in oil which may affect absorption and metabolism; high concentrations were used; a time-weighted average dose was reported; however, doses causing toxic responses were often administered cyclically (one week, no treatment, followed by four weeks of treatment, five days/week); during some experiments dose levels were lowered or raised; for criteria calculations, doses administered five days/week were adjusted to an average daily dose as if administered seven days/week.

Under the Consent Decree in NRDC vs. 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." 1,2-Dichloroethane, 1,1,2-trichloroethane, 1,1,2,2-tetrachloroethane and hexachloroethane are suspected of being human carcinogens. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of these chlorinated ethanes in water for maxiumum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of these chlorinated ethanes 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 at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure Assumptions	Risk Levels and Corresponding Criteria (1)			
	0	10^{-7}	10^{-6}	10^{-5}
2 liters of drinking water and consumption of 18.7 grams of fish and shellfish (2)				
1,2-dichloroethane	0	0.07 µg/l	0.07 µg/l	7.0 µg/l
1,1,2-trichloroethane	0	0.027 µg/l	0.27 µg/l	2.7 µg/l
1,1,2,2-tetrachloroethane	0	0.018 µg/l	0.18 µg/l	1.8 µg/l
hexachloroethane	0	0.059 µg/l	0.59 µg/l	5.9 µg/l
Consumption of fish and shellfish only.				
1,2-dichloroethane	0	1.708 µg/l	17.08 µg/l	170.8 µg/l
1,1,2-trichloroethane	0	0.483 µg/l	4.83 µg/l	48.3 µg/l
1,1,2,2-tetrachloroethane	0	0.127 µg/l	1.27 µg/l	12.7 µg/l
hexachloroethane	0	0.079 µg/l	0.79 µg/l	7.9 µg/l

(1) Calculated by applying a modified "one hit" extrapolation model described in the FR 15926, 1979. Appropriate bioassay data used in the calculation of the model are presented

in Appendix I. Since the extrapolation model is linear to 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) Four percent of 1,2-dichloroethane exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 4.6 fold. The remaining 96 percent of 1,2-dichloroethane exposure results from drinking water.

Six percent of 1,1,2-trichloroethane exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 6.3 fold. The remaining 94 percent of 1,1,2-trichloroethane exposure results from drinking water.

Fourteen percent of 1,1,2,2-tetrachloroethane exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 18 fold. The remaining 86 percent of 1,1,2,2-tetrachloroethane exposure results from drinking water.

Seventy-five percent of hexachloroethane exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 320 fold. The remaining 25 percent of hexachloroethane exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of these chlorinated ethanes (1) occurring from the consumption of both drinking water and aquatic life grown in water containing the corresponding chlorinated ethane concentrations and, (2) occurring solely from the consumption of aquatic life grown in the waters containing the corresponding chlorinated ethane concentrations.

Although total exposure information for the above chlorinated ethanes is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into the ambient water quality criteria formulation because of the tenuous estimates. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

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APPENDIX I

Summary and Conclusions Regarding the Carcinogenicity of Chlorinated Ethanes*

Chlorinated ethanes are used extensively as solvents and as intermediates in chemical syntheses. They have been detected in U.S. drinking water supplies and in finished drinking water. Chlorinated ethanes, which have been detected in water, include 1,1- 1,2-dichloroethanes, 1,1,1- and 1,1,2-trichloroethanes, and 1,1,1,2-tetrachloroethane.

Four of the nine chlorinated ethanes are known animal carcinogens. They are 1,2-dichloroethane, 1,1,2-trichloroethane, 1,1,2,2,-tetrachloroethane and hexachloroethane (NCI, 1978a,b,c,d). Carcinogenesis testing of 1,1,1-trichloroethane (retesting), 1,1,1,2-tetrachloroethane and pentachloroethane is in progress at the National Cancer Institute (NCI). Carcinogenesis testing is planned for chloroethane (NCI, 11/79).

Chlorinated ethanes produce a variety of cancers in rats and mice, receiving oral doses of these chemicals. 1,2-Dichloroethane, administered by gavage over a period of 78 weeks, produced squamous cell carcinomas of the stomach (107 mg/kg/day) and hemangiosarcomas (54 mg/kg/day) in male Osborne-Mendel rats. Nine of 50 animals (18 percent) developed stomach cancers and 7 of 50 animals (14 percent) developed hemangiomas. None of the twenty control animals developed either cancer type. Female Osborne-Mendel

*This summary has been prepared and approved by the Carcinogens Assessment Group, EPA, on July 17, 1979.

rats (95 mg/kg/day) and B6C3F1 mice (149 mg/kg/day) developed adenocarcinomas of the mammary gland (NCI, 1978a). Eighteen of 50 treated rats (36 percent) and 9 of 50 treated mice (18 percent) developed mammary cancers. Adenocarcinomas of the mammary gland were not observed in 20 vehicle-treated controls of both species.

1,1,2-trichloroethane, administered by gavage over a period of 78 weeks induced hepatocellular carcinomas in male (195 and 390 mg/kg/day) and female (195 mg/kg/day and 390 mg/kg/day) B6C3F1 mice (NCI, 1978b). Tumor incidences in treated males were 37/49 (76 percent) and 18/49 (37 percent) at the high and low doses respectively, as compared to 2/20 (10 percent) in the vehicle-treated controls. Tumor incidences in treated females were 40/45 (89 percent) and 16/48 (33 percent) at the high and low doses, respectively, as compared to no observed cancers in twenty vehicle controls.

1,1,1-trichloroethane is being retested at the NCI because high mortality rates among animals, in an earlier carcinogenesis bioassay, made it impossible to assess the carcinogenicicty ingested 1,1,1-trichloroethane, even though a variety of neoplasms was observed (NCI,1977). In another study, 1,1,1-trichloroethane induced the transformation of rat embryo cells and the transformed cells, when injected into newborn Fischer rats, produced fibrosarcomas at the site of injection in all treated animals (Price, et al. 1978).

1,1,2,2-tetrachloroethane is carcinogenic to B6C3F1 mice. This chemical, given by gavage, in average doses

of 142 mg/kg/day and 284 mg/kg/day over a period of 78 weeks, induced hepatocellular carcinomas in male and female mice (NCI, 1978c). Tumor incidences in males were 44/49 (90 percent), 13/50 (26 percent), and 1/18 (5 percent) in the high dose, low dose, and vehicle control groups, respectively. Tumor incidences in females were 43/49 (91 percent), 30/48 (63 percent), and 0/20 in high dose, low dose, and vehicle control groups, respectively.

In addition to its use as a solvent, hexachloroethane is used as a veterinary anthelmitic. This chemical has demonstrated carcinogenic activity in both male and female B6C3F1 mice. Thirty-one of 49 treated male mice (63 percent) developed hepatocellular carcinomas after receiving average oral doses of 1,179 mg/kg/day over a 78-week period as compared to 3 of 20 vehicle-treated controls (15 percent). Twenty of 50 female mice (40 percent) developed hepatocellular carcinomas after receiving average oral doses of 590 mg/kg/day hexachloroethane as compared to 2 of 20 (10 percent) vehicle-treated controls.

Two chlorinated ethanes are known mutagens. 1,2-Dichloroethane and 1,1,2,2-tetrachloroethane were mutagenic in the Ames Salmonella assay for strains TA 1530 and 1535, and for the E. coli DNA polymerase-deficient system (Brem, et al. 1974). Rosenkranz (1977) determined the order of mutagenic activity toward S. typhimurium and E. coli to be 1,1,2,2-tetrachloroethane > 1,2-dichloroethane. 1,2-Dichloroethane induced highly significant increases in somatic mutation frequencies in Drosophila melangaster (Nylander, et al.

1978). Morphological and chlorophyll mutations in eight varietites of peas were induced by treatment of seeds with 1,2-dichloroethane (Kirichek, 1974).

A conjugation product of 1,2-dichloroethane, S-chloroethyl cystein, proved to be more mutagenic than the parent compound (Rannug, et al. 1978). Other metabolites of 1,2-dichloroethane varied in their mutagenic activity for Salmonella strains. 2-Chloroacetaldehyde was mutagenic for strain TA 100 (McCann, et al. 1975), strains TA 1530 and TA 1535 (Rannug, et al. 1978). 2-Chloroethanol was less mutagenic than the aldehyde derivative and 2-chloroacetic acid was inactive (McCann, et al. 1975).

Hexachloroethane was not mutagenic for five strains of Salmonella or yeast (Sacchyaromyces cerevisiae D^4) in the absence or presence of induced rat liver S-9 preparations (Weeks, et al. 1979).

No data were found regarding the mutagenic potential of chloroethane, 1,1-dichloroethane, 1,1,1- and 1,1,2-trichloroethanes, 1,1,1,2-tetrachloroethane or pentachloroethane.

The demonstrated carcinogenicity of 1,2-dichloroethane, 1,1,2-trichloroethane, 1,1,1,2-tetrachloroethane and hexachloroethane coupled with the mutagenicity data constitutes strong evidence that these chemicals are likely to be human carcinogens.

The water quality criterion for 1,2-dichloroethane is based on the induction of mammary adenocarcinomas in female Osborne-Mendel rats, given average oral doses of 197 mg/kg/day 1,2-dichloroethane over a period of 78 weeks (NCI, 1978a). The concentration of 1,2-dichloroethane in

water, calculated to keep the lifetime cancer risk below 10^{-5} is 7.0 μg/l.

The water quality criterion for 1,1,2-trichloroethane is based on the induction of hepatocellular carcinomas in female B6C3F1 mice, given an average oral dose of 390 mg/kg/day over a 78-week period (NCI, 1978b). The concentration of 1,1,2-trichloroethane in water, calculated to keep the lifetime cancer risk below 10^{-5} is 2.7 μg/l.

The water quality crterion for 1,1,2,2-tetrachloroethane is based on the induction of hepatocellular carcinomas in male B6C3F1 mice, receiving average oral doses of 284 mg/kg/day over a 78-week period (NCI, 1978c). The concentration of 1,1,2,2-tetrachloroethane in water, calculated to keep the lifetime cancer risk below 10^{-5} is 1.8 μg/l.

The water quality criterion for hexachloroethane is based on the induction of hepatocellular carcinomas in male B6C3F1 mice, given an average oral dose of 1,179 mg/kg/day over a 78-week period (NCI, 1978d). The concentration of hexachloroethane in water, calculated to keep the lifetime cancer risk below 10^{-5} is 5.9 μg/l.

Because carcinogenicity data are lacking for chloroethane, 1,1-dichloroethane, 1,1,1-trichloroethane, 1,1,1,2-tetrachloroethane, and pentachloroethane, water quality criteria based on a 10^{-5} risk level cannot be derived.

Summary of Pertinent Data for 1,2-Dichloroethane

The water quality criterion for 1,2-dichloroethane is based on the induction of mammary adenocarcinomas in female Osborne-Mendel rats, given an average oral dose of 107 mg/kg/day 1,2-dichloroethane over a period of 78 weeks (NCI, 1978a). The incidences of mammary adenocarcinomas were 18/50 and 0/20 in the treated and control groups, respectively. The criterion was calculated from the following parameters:

n_t = 18 d = 76.4 mg/kg/day (107 mg/kg/day x 5/7)

N_t = 50 f = 0.0187 kg/day

n_c = 0 R = 4.6

N_c = 20 w = 0.319 kg

Le = 110 wks.

le = 69 wks.

L = 110 wks.

Based on these parameters, the one-hit slope (B_H) is 0.04765 $(mg/kg/day)^{-1}$. The concentration of 1,2-dichloroethane in water, calculated to keep the lifetime cancer risk below 10^{-5} is 7.0 µg/l.

Summary of Pertinent Data for 1,1,2-trichloroethane

The water quality criterion for 1,1,2-trichloroethane is based on the induction of hepatocellular carcinomas in female B6C3F1 mice, given an average oral dose of 390 mg/kg/day over a 78 week period (NCI, 1978b). The incidences of hepatocellular were 40/45 and 0/20 in the treated and control groups, respectively. The criterion was calculated from the following parameters:

n_t = 40 d = 279 mg/kg/day (390 mg/kg/day x 5/7)

N_t = 45 F = 0.0187 kg/day

n_c = 0 R = 6.3

N_c = 20 w = 0.029 kg

Le = 91 wks

le = 78 wks

L = 91 wks

Based on these parameters, the one-hit slope (B_H) is 0.123 $(mg/kg/day)^{-1}$. The concentration of 1,1,2-trichloroethane in water, calculated to keep the lifetime cancer risk below 10^{-5} is 2.7 µg/l.

Summary of Pertinent Data for 1,1,2,2-Tetrachloroethane

The water quality criterion for 1,1,2,2-tetrachloroethane is based on the induction of hepatocellular carcinomas in male B6C3F1 mice, receiving average oral doses of 284 mg/kg/day over a 78-week period (NCI, 1978c). The incidences of hepatocellular carcinomas were 44/49 and 1/18 in the treated and control groups, respectively. The criterion was calculated from the following parameters:

n_t = 44 d = 203 mg/kg/day (284 mg/kg/day x 5/7)

N_t = 49 F = 0.0187 kg/day

n_c = 1 R = 18

N_c = 18 w = 0.035 kg

Le = 91 wks

le = 78 wks

L = 91 wks

Based on these parameters, the one-hit slope (B_H) is 0.1638 $(mg/kg/day)^{-1}$. The concentration of 1,1,2,2-tetrachloroethane in water, calculated to keep the lifetime cancer risk below 10^{-5}, is 1.8 µg/l.

Summary of Pertinent Data for Hexachloroethane

The water quality criterion for hexachloroethane is based on the induction of hepatocellular carcinomas in male B6C3F1 mice, given an average oral dose of 1,179 mg/kg/day over a 78-week period (NCI, 1978d). The incidences of hepatocellular carcinomas were 31/49 and 3/20 in the treated and control groups, respectively. The criterion was calculated from the following parameters:

n_t = 31 d = 842 mg/kg/day (1179 mg/kg/day x 5/7)

N_t = 49 F = 0.0187 kg/day

n_c = 3 R = 320

N_c = 20 w = 0.032 kg

Le = 91 wks

le = 78 wks

L = 91 wks

Based on these parameters, the one-hit slope (B_H) is 0.0149 $(mg/kg/day)^{-1}$. The concentration of hexachloroethane in water, calculated to keep the lifetime cancer risk below 10^{-5}, is 5.9 µg/l.