United States
Environmental Protection
Agency

Office of Water
Regulations and Standards
Criteria and Standards Division
Washington DC 20460

EPA 440/5-80-043
October 1980

c. 1

EPA

Ambient Water Quality Criteria for Dichloropropane and Dichloropropene

AMBIENT WATER QUALITY CRITERIA FOR

DICHLOROPROPANES/DICHLOROPROPENES

Prepared By
U.S. ENVIRONMENTAL PROTECTION AGENCY

Office of Water Regulations and Standards
Criteria and Standards Division
Washington, D.C.

Office of Research and Development
Environmental Criteria and Assessment Office
Cincinnati, Ohio

Carcinogen Assessment Group
Washington, D.C.

Environmental Research Laboratories
Corvalis, Oregon
Duluth, Minnesota
Gulf Breeze, Florida
Narragansett, Rhode Island

DISCLAIMER

This report has been reviewed by the Environmental Criteria and Assessment Office, U.S. Environmental Protection Agency, and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

AVAILABILITY NOTICE

This document is available to the public through the National Technical Information Service, (NTIS), Springfield, Virginia 22161.

ENVIRONMENTAL PROTECTION AGENCY

FOREWORD

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

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

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

STEVEN SCHATZOW
Deputy Assistant Administrator
Office of Water Regulations and Standards

ACKNOWLEDGEMENTS

Aquatic Life Toxicology:

William A. Brungs, ERL-Narragansett
U.S. Environmental Protection Agency

David J. Hansen, ERL-Gulf Breeze
U.S. Environmental Protection Agency

Mammalian Toxicology and Human Health Effects:

S. L. Schwartz (author)
Georgetown University School of Medicine

Christopher T. DeRosa (doc. mgr.)
ECAO-Cin
U. S. Environmental Protection Agency

Donna Sivulka (doc. mgr.)
ECAO-Cin
U. S. Environmental Protection Agency

Robert Donner, HERL
U. S. Environmental Protection Agency

Larry Fishbein
National Center for Toxicological Research

Terri Laird
ECAO-Cin
U. S. Environmental Protection Agency

Chad Sandusky
U. S. Environmental Protection Agency

Benjamin L. Van Duuren
New York University Medical Center

Jerry F. Stara
ECAO-Cin
U. S. Environmental Protection Agency

Julian Andelman
University of Pittsburgh

Richard A. Carchman
Medical College of Virginia

Jaqueline V. Carr
U. S. Environmental Protection Agency

Patrick Durkin
Syracuse Research Corporation

Rolf Hartung
University of Michigan

Si Duk Lee
ECAO-Cin
U. S. Environmental Protection Agency

Joseph Santodonato
Syracuse Research Corporation

Yin-tak Woo

Technical Support Services Staff: D.J. Reisman, M.A. Garlough, B.L. Zwayer, P.A. Daunt, K.S. Edwards, T.A. Scandura, A.T. Pressley, C.A. Cooper, M.M. Denessen.

Clerical Staff: C.A. Haynes, S.J. Faehr, L.A. Wade, D. Jones, B.J. Bordicks, B.J. Quesnell, T. Highland, R. Rubinstein.

TABLE OF CONTENTS

	Page
Criteria Summary	
Introduction	A-1
Aquatic Life Toxicology	B-1
Introduction	B-1
Effects	B-1
Acute Toxicity	B-1
Chronic Toxicity	B-2
Plant Effects	B-3
Miscellaneous	B-4
Summary	B-4
Criteria	B-5
References	B-11
Mammalian Toxicology and Human Health Effects	C-1
Introduction	C-1
Exposure	C-3
Ingestion from Water	C-3
Ingestion from Food	C-3
Inhalation	C-4
Dermal	C-7
Pharmacokinetics	C-7
Effects (Dichloropropane)	C-10
Acute, Subacute and Chronic Toxicity	C-10
Mutagenicity	C-16
Carcinogenicity	C-18
Effects (Dichloropropene)	C-18
Acute, Subacute and Chronic Toxicity	C-18
Mutagenicity	C-20
Carcinogenicity	C-23
Effects (Dichloropropane/Dichloropropene Mixtures)	C-23
Acute, Subacute and Chronic Toxicity	C-23
Mutagenicity	C-25
Carcinogenicity	C-25
Criterion Formulation	C-25
Dichloropropanes (PDC)	C-26
Dichloropropenes (DCP)	C-27
Summary	C-28
References	C-29

CRITERIA DOCUMENT

DICHLOROPROPANES/DICHLOROPROPENES

CRITERIA

Aquatic Life

The available data for dichloropropanes indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 23,000 and 5,700 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for dichloropropene indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 6,060 and 244 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for dichloropropane indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 10,300 and 3,040 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for dichloropropene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 790 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of dichloropropene to sensitive saltwater aquatic life.

Human Health

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for dichloropropanes.

For the protection of human health from the toxic properties of dichloropropenes ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 87 μg/l.

For the protection of human health from the toxic properties of dichloropropenes ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 14.1 mg/l.

INTRODUCTION

Principal uses of dichloropropanes and dichloropropenes are as soil fumigants for the control of nematodes, in oil and fat solvents, and in dry cleaning and degreasing processes (Windholz, 1976). Dichloropropanes and dichloropropenes can enter the aquatic environment as discharges from industrial effluents, by runoff from agricultural land, and from municipal effluents. These compounds have been detected in New Orleans drinking water, although they were not quantified (Dowty, et al. 1975). Most data on persistence, degradation, and distribution of dichloropropanes and dichloropropenes deal with their presence in soils.

Dichloropropanes and dichloropropenes are liquids at environmental temperatures and have molecular weights of 112.99 and 110.97, respectively (Weast, 1977). Composition of specific compounds are shown in Table 1.

Lange (1952) reports a water solubility of 270 mg/100 ml at 20°C for 1,2-dichloropropane. The vapor pressure of 1,2-dichloropropane is 40 mm Hg at 19.4°C (Sax, 1975). A review of various fumigants, fungicides, and nematocides by Goring and Hamaker (1972) lists the water solubility at 20°C as 0.27 percent for cis-1,3-dichloropropene and 0.28 percent for trans-1,3-dichloropropene.

Mixtures of 1,2-dichloropropane and cis- and trans-1,3-dichloropropene are used as soil fumigants. When heated to decomposition, 1,2-dichloropropane emits highly toxic fumes of phosgene, while 1,3-dichloropropene gives off toxic fumes of chlorides (Sax, 1975).

Dichloropropenes have been shown to undergo photochemical formation of free radicals (Richerzhagen, et al. 1973). The cis- and trans-isomers of

TABLE 1

Some Physical Properties of Dichloropropanes and Dichloropropenes*

Dichloropropanes	Boiling point (°C)	Density	Dichloropropenes	Boiling point (°C)	Density
1,1-PDC	88.1	1.132	1,1-DCP	76-77	1.186
1,2-PDC	96.4	1.156	1,2(cis)-DCP		
1,3-PDC	120.4	1,188	1,3(trans)-DCP	77	1.182
2,2-PDC	69.3	1.112	1,3(cis)-DCP	104.3	1.217
			1,3-(trans)-DCP	112	1.224

*Source: Weast, 1977

1,3-dichloropropene have undergone biodehalogenation by a Pseudomonas species isolated from the soil (Belser and Castro, 1971). 1,3-Dichloropropene has been shown to react with biological materials (cow's milk, potatoes, humus-rich soil) to produce 3-chloroallyl methyl sulfide (Dekker, 1972).

In the nonaquatic environment, movement of dichloropropene and dichloropropane in the soil results from diffusion in the vapor phase, as these compounds tend to establish an equilibrium between concentrations in vapor, water, and absorbing phases (Leistra, 1970). Degradation of some of these compounds can occur in the soil. Van Dijk (1974) reports that cis- and trans-1,3-dichloropropene can be chemically hydrolyzed in moist soils to the corresponding 3-chloroalkyl alcohols, which are capable of metabolizing to carbon dioxide and water by a bacterium (Pseudomonas sp.). Although field applications of 1,3-dichloropropene have shown between 15 and 80 percent decomposition (Van Dijk, 1974), the large amount that can be absorbed (80 to 90 percent) can result in considerable residues existing months after application is completed (Leistra, 1970). 1,2-Dichloropropane, however, appears to undergo minimal degradation in the soil, with the major route of dissipation appearing to be volatilization (Roberts and Stoydin, 1976). The persistence and degradation of dichloropropanes and dichloropropenes depends on susceptibility to hydrolysis (Thomason and McKenry, 1973), soil types (Leistra, 1970), and temperature (Van Dijk, 1974; Thomason and McKenry, 1973). For example, cis-DCP is chemically hydrolyzed in moist soils to the corresponding cis-3-chloroallyl alcohol, which can be microbially degraded to carbon dioxide and water by Pseudomonas sp. (Van Dijk, 1974).

The distribution of PDC and DCP within soils depends upon soil conditions. These same conditions in turn influence their potential as persistent health hazards as soil contaminants potentially toxic to developing crop plants. When Telone® is applied to a moist, warm soil at a rate of

234 l/ha, cis-DCP can be expected to remain in the soil at concentrations greater than 10 μg/l for two to four months, depending on the soil type (Thomason and McKenry, 1973). Under certain conditions, developing roots and tubers of crop plants can absorb small quantities of the remaining compounds (Williams, 1968). However, fumigation of sandy soils with relatively low dosage of alkyl nematocides under proper conditions produced no residues of nematocides and had no adverse effects on the flavor or nutritional value of lima beans, carrots, or citrus fruits (Emerson, et al. 1969). These were the only food crops tested. No information was found concerning the concentrations of the PDC and DCP in commercial foodstuffs. Thus, the amount of these compounds ingested by humans through food is not known.

REFERENCES

Belser, N.O. and C.E. Castro. 1971. Biodehalogenation: Metabolism of the nematocides cis- and trans-3-chloroallyl alcohol by a bacterium isolated from soil. Jour. Agric. Food Chem. 19: 23.

Dekker, W.H. 1972. 3-Chlorallyl methyl sulfide, a product from the reaction of 1,3-dichloropropene and biological materials. Medea, Fac. Andbouwawetensch., Ryksania. Geal. 37: 865.

Dowty, B., et al. 1975. Halogenated hydrocarbons in New Orleans drinking water and blood plasma. Science. 87: 75.

Emerson, G.A., et al. 1969. Effects of soil fumigants on the quality and nutritive value of selected fruits and vegetables. VIII. International Nutritonal Congress Symposium. Sept. 2. Prague, Czechoslovakia.

Goring, C.A.I. and J.W. Hamaker. 1972. Organic chemicals in the soil environment. Environment. Marcel Dekker, Inc., New York.

Lange, N.A. 1952. Lange's Handbook of Chemistry. 8th ed. Handbook Publishers, Inc., Sandusky, Ohio.

Leistra, M. 1970. Distribution of 1,3-dichloropropene over the phases in soil. Jour. Agric. Food Chem. 18: 1124.

Richerzhagen, T., et al. 1973. Photochemical formulation of free radicals from chlorolefins as studied by electron spin resonance. Jour. Phys. Chem. 77: 1819.

Roberts, R.T. and G. Stoydin. 1976. The degradation of (Z)- and (E)-1,3-dichloropropenes and 1,2-dichloropropanes in soil. Pestic. Sci. 7: 325.

Sax, N.I. 1975. Dangerous Properties of Industrial Materials. Reinhold Book Corp., New York.

Thomason, I.J. and M.V. McKenry. 1973. Part I. Movement and fate as affected by various conditions in several soils. Halgardia. 42: 393.

Van Dijk, H. 1974. Degradation of 1,3-dichloropropenes in soil. Agro-Ecosystems. 1: 193.

Weast, R.C. (ed.) 1977. Handbook of Chemistry and Physics. 58th ed. CRC Press, Inc., Cleveland, Ohio.

Williams, I.H. 1968. Recovery of cis- and trans-1,3-dichloropropene residues from two types of soils and their detection and determination by electron capture gas chromotography. Jour. Econ. Bnt. 61: 1432.

Windholz, M. (ed.) 1976. The Merck Index. 9th ed. Merck and Co., Inc., Rahway, New Jersey.

Aquatic Life Toxicology*

INTRODUCTION

The available freshwater aquatic life data for these two classes of compounds with one exception are for dichloropropanes. Where data exist for both 1,3-dichloropropene and 1,3-dichloropropane tested under similar conditions, the propene is much more toxic than the propane.

The data base for dichloropropanes and dichloropropenes and saltwater organisms is limited to studies with 1,2- and 1,3-dichloropropane, and 1,3-dichloropropene. Toxicity tests with saltwater organisms have not been done on other chemicals in these classes; and effects of salinity, temperature, or other water quality factors on toxicity are unknown.

EFFECTS

Acute Toxicity

Daphnia magna is the only freshwater invertebrate species tested with these classes of compounds (Table 1). Under static test conditions the 48-hour EC_{50} values for 1,1-, 1,2-, and 1,3-dichloropropane were 23,000, 52,500, and 282,000 µg/l, respectively (U.S. EPA, 1978). The 48-hour EC_{50} value for 1,3-dichloropropene under static test conditions is 6,150 µg/l (U.S. EPA, 1978). This compound is 46 times more toxic than 1,3-dichloropropane.

The bluegill was also exposed to 1,1-, 1,2-, and 1,3-dichloropropane under similar conditions and yielded 96-hour LC_{50} values of 97,900, 300,000, and greater than 520,000 µg/l (Tables 1 and 4), respectively (U.S. EPA, 1978). The 96-hour LC_{50} values for fathead minnows tested under flow-

---

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

through conditions with measured concentrations are 139,300 and 131,100 µg/l for 1,2-dichloropropane and 1,3-dichloropropane, respectively.

From these tests it appears that toxicity generally decreases as the distance between the chlorine atoms increases with 1,2- being less toxic than 1,1-dichloropropane. This was true for Daphnia magna also. Dawson, et al. (1977) reported a 96-hour LC_{50} value of 320,000 µg/l for bluegill exposed to 1,2-dichloropropane; this result is similar to that previously mentioned for that species.

The 96-hour LC_{50} value for 1,3-dichloropropene is 6,060 µg/l for bluegill (U.S. EPA, 1978). This LC_{50} value is approximately two orders of magnitude lower than that for 1,3-dichloropropane.

Mysidopsis bahia, the only saltwater invertebrate species acutely tested, was more sensitive than the fishes (Table 1). For mysid shrimp, 1,3-dichloropropene (96-hour LC_{50} = 790 µg/l) was 13 times more toxic than 1,3-dichloropropane (96-hour LC_{50} = 10,300 µg/l); this is in agreement with the conclusion drawn from the data (Table 1) for Daphnia magna.

The 96-hour LC_{50} values (Table 1) were 240,000 µg/l for the tidewater silverside and 1,2-dichloropropane (Dawson, et al. 1977); for the sheepshead minnow the values were 86,700 µg/l for 1,3-dichloropropane and 1,770 µg/l for 1,3-dichloropropene (U.S.EPA, 1978). The LC_{50} value for 1,3-dichloropropane is 49 times greater than that for 1,3-dichloropropene. The LC_{50} value for 1,2-dichloropropane and the tidewater silverside is much greater than those for 1,3-dichloropropane and 1,3-dichloropropene and the sheepshead minnow, but it is impossible to tell whether the difference is due to different toxicities of the chemicals or responses of the species.

Chronic Toxicity

Embryo-larval tests have been conducted with the fathead minnow and 1,2- and 1,3-dichloropropane and 1,3-dichloropropene (Table 2). As was true in

the acute toxicity tests, the propene was much more toxic. Two tests were conducted with 1,2-dichloropropane and the chronic values are 60,000 µg/l (U.S. EPA, 1978) and 8,100 µg/l (U.S. EPA, 1980). No cause for this difference is known. The chronic values for 1,3-dichloropropane and 1,3-dichloropropene and the fathead minnow are 5,700 and 244 µg/l, respectively. As was found with the acute toxicity data, 1,3-dichloropropene was much more toxic than 1,3-dichloropropane.

Only one study on chronic toxicity of dichloropropanes and dichloropropenes to saltwater organisms using measured concentrations has been found (Table 2). In a life-cycle study with the mysid shrimp, the chronic value for 1,3-dichloropropane was 3,040 µg/l (U.S. EPA, 1978). Using this datum and that in Table 1 from the same study, an acute-chronic ratio of 3.4 is obtained.

An embryo-larval test with the sheepshead minnow and 1,2-dichloropropane has been conducted (U.S. EPA, 1978); however, the test concentrations were not measured. The highest no effect concentration was 82,000 µg/l and there was a significant effect on growth at 164,000 µg/l (Table 4).

Plant Effects

For 1,3-dichloropropene, the 96-hour EC_{50} values, based on chlorophyll *a* and cell numbers of the freshwater alga, *Selenastrum capricornutum*, were 4,950 and 4,960 µg/l, respectively (Table 3). The respective values for 1,3-dichloropropane were 48,000 and 72,200 µg/l. Thus the propene is much more toxic than the propane, as was true with the fish and invertebrate species.

The saltwater alga, *Skeletonema costatum*, was as sensitive to 1,3-dichloropropene (Table 3) as fishes and mysid shrimp. The 96-hour EC_{50} value for growth, based on concentrations of chlorophyll *a* in culture, was 1,000 µg/l. The EC_{50} calculated from cell numbers was 1,040 µg/l.

As with fishes and mysids, 1,3-dichloropropane was less toxic than 1,3-dichloropropene to Skeletonema costatum. The 96-hour EC_{50} value from data for chlorophyll a was 65,800 µg/l; for cell number it was 93,600 µg/l.

There were no data reported in the literature on effects of dichloropropanes or dichloropropenes on freshwater or saltwater vascular plants.

Miscellaneous

In a test conducted on a mixed assemblage of emerald shiners and fathead minnows exposed to 1,3-dichloropropene (Scott and Wolf, 1962), 100 percent of the fish survived three days at 1,000 µg/l, and none survived at 10,000 µg/l (Table 4). This is in general agreement with the value of 6,060 µg/l for the 96-hour LC_{50} value for the bluegill (U.S. EPA, 1978).

Summary

There may be a general pattern of decreased acute toxicity as the distance between the chlorine atoms increases for the dichloropropanes and two freshwater species. The 48-hour EC_{50} values for Daphnia magna ranged from 23,000 to 282,000 µg/l for 1,1-, 1,2-, and 1,3-dichloropropane. For the same sequence of chemicals, the 96-hour LC_{50} values for the bluegill range from 97,900 to greater than 520,000 µg/l. Chronic values for the fathead minnow were 60,000 and 8,100 µg/l for 1,2-dichloropropane and 5,700 µg/l for 1,3-dichloropropane. The lowest 96-hour EC_{50} values for the alga, Selenastrum capricornutum, were 4,950 and 48,000 µg/l for 1,3-dichloropropene and 1,3-dichloropropane, respectively. In both acute and chronic tests with freshwater organisms, 1,3-dichloropropene was one to two orders of magnitude more toxic than 1,3-dichloropropane.

Most of the saltwater data are for 1,3-dichloropropane and 1,3-dichloropropene. The propene was much more toxic to the mysid shrimp and sheepshead minnow, with 96-hour LC_{50} values of 790 and 1,770 µg/l, respectively, than

the propane with 96-hour LC_{50} values of 10,300 µg/l for the shrimp and 86,700 µg/l for the minnow. The chronic value for 1,3-dichloropropane and the mysid shrimp was 3,040 µg/l, which provides an acute-chronic ratio of 3.4. The saltwater alga, Skeletonema costatum, had 96-hour EC_{50} values of 1,000 and 1,040 µg/l for 1,3-dichloropropene and 65,800 and 93,600 µg/l for 1,3-dichloropropane.

CRITERIA

The available data for dichloropropanes indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 23,000 and 5,700 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for dichloropropene indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 6,060 and 244 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for dichloropropane indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 10,300 and 3,040 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for dichloropropene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 790 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of dichloropropene to sensitive saltwater aquatic life.

Table 1. Acute values for dichloropropanes-dichloropropenes

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Acute Value (µg/l)	Reference
		FRESHWATER SPECIES			
Cladoceran, *Daphnia magna*	S, U	1,1-dichloro-propane	23,000	23,000	U.S. EPA, 1978
Cladoceran, *Daphnia magna*	S, U	1,2-dichloro-propane	52,500	52,500	U.S. EPA, 1978
Cladoceran, *Daphnia magna*	S, U	1,3-dichloro-propane	282,000	282,000	U.S. EPA, 1978
Cladoceran, *Daphnia magna*	S, U	1,3-dichloro-propene	6,150	6,150	U.S. EPA, 1978
Fathead minnow, *Pimephales promelas*	FT, M	1,2-dichloro-propane	139,300	139,300	U.S. EPA, 1980
Fathead minnow, *Pimephales promelas*	FT, M	1,3-dichloro-propane	131,100	131,100	U.S. EPA, 1980
Bluegill, *Lepomis macrochirus*	S, U	1,1-dichloro-propane	97,900	97,900	U.S. EPA, 1978
Bluegill, *Lepomis macrochirus*	S, U	1,2-dichloro-propane	320,000	-	Dawson, et al. 1977
Bluegill, *Lepomis macrochirus*	S, U	1,2-dichloro-propane	280,000	300,000	U.S. EPA, 1978
Bluegill, *Lepomis macrochirus*	S, U	1,3-dichloro-propene	6,060	6,060	U.S. EPA, 1978
		SALTWATER SPECIES			
Mysid shrimp, *Mysidopsis bahia*	S, U	1,3-dichloro-propene	790	790	U.S. EPA, 1978
Mysid shrimp, *Mysidopsis bahia*	S, U	1,3-dichloro-propane	10,300	10,300	U.S. EPA, 1978

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50 (µg/l)	Species Acute Value (µg/l)	Reference
		SALTWATER SPECIES			
Sheepshead minnow, *Cyprinodon variegatus*	S, U	1,3-dichloro-propene	1,770	1,770	U.S. EPA, 1978
Sheepshead minnow, *Cyprinodon variegatus*	S, U	1,3-dichloro-propane	86,700	86,700	U.S. EPA, 1978
Tidewater silverside, *Menidia beryllina*	S, U	1,2-dichloro-propane	240,000	240,000	Dawson, et al. 1977

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

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

Table 2. Chronic values for dichloropropanes-dichloropropenes

Species	Method*	Chemical	Limits (µg/l)	Chronic Value (µg/l)	Reference
		FRESHWATER SPECIES			
Fathead minnow, *Pimephales promelas*	E-L	1,2-dichloro-propane	40,000-91,000	60,000	U.S. EPA, 1978
Fathead minnow, *Pimephales promelas*	E-L	1,2-dichloro-propane	6,000-11,000	8,100	U.S. EPA, 1980
Fathead minnow, *Pimephales promelas*	E-L	1,3-dichloro-propane	4,000-8,000	5,700	U.S. EPA, 1980
Fathead minnow, *Pimephales promelas*	E-L	1,3-dichloro-propene	180-330	244	U.S. EPA, 1978
		SALTWATER SPECIES			
Mysid shrimp, *Mysidopsis bahia*	LC	1,3-dichloro-propane	2,200-4,200	3,040	U.S. EPA, 1978

* E-L = embryo-larval, LC = partial life cycle or full life cycle

Acute-Chronic Ratio

Species	Chemical	Chronic Value (µg/l)	Acute Value (µg/l)	Ratio
Fathead minnow, *Pimephales promelas*	1,2-dichloro-propane	8,100	139,300	17
Fathead minnow, *Pimephales promelas*	1,2-dichloro-propane	60,000	139,300*	2.3
Fathead minnow, *Pimephales promelas*	1,3-dichloro-propane	5,700	131,100	23
Mysid shrimp, *Mysidopsis bahia*	1,3-dichloro-propane	3,040	10,300	3.4

* This acute value is from a different study (ERL-D, 1980) but was used here because the study (U.S. EPA, 1978) that provided the chronic value of 60,000 ug/l did not include an acute test with this species.

Table 3. Plant values for dichloropropanes-dichloropropenes (U.S. EPA, 1978)

Species	Chemical	Effect	Result (µg/l)
	FRESHWATER SPECIES		
Alga, *Selenastrum capricornutum*	1,3-dichloro-propene	Chlorophyll *a* 96-hr EC50	4,950
Alga, *Selenastrum capricornutum*	1,3-dichloro-propene	Cell numbers 96-hr EC50	4,960
Alga, *Selenastrum capricornutum*	1,3-dichloro-propane	Chlorophyll *a* 96-hr EC50	48,000
Alga, *Selenastrum capricornutum*	1,3-dichloro-propane	Cell numbers 96-hr EC50	72,200
	SALTWATER SPECIES		
Alga, *Skeletonema costatum*	1,3-dichloro-propene	Chlorophyll *a* 96-hr EC50	1,000
Alga, *Skeletonema costatum*	1,3-dichloro-propene	Cell number 96-hr EC50	1,040
Alga, *Skeletonema costatum*	1,3-dichloro-propane	Chlorophyll *a* 96-hr EC50	65,800
Alga, *Skeletonema costatum*	1,3-dichloro-propane	Cell number 96-hr EC50	93,600

Table 4. Other data for dichloropropanes-dichloropropenes

Species	Chemical	Duration	Effect	Result (µg/l)	Reference
		FRESHWATER SPECIES			
Mixed group of Emerald shiner, *Notropis atherinoides* and Fathead minnow, *Pimephales promelas*	1,3-dichloropropene	3 days	Mortality	100% survival at 1,000 100% mortality at 10,000	Scott & Wolf, 1962
Bluegill, *Lepomis macrochirus*	1,3-dichloropropane	96 hrs	LC50	>520,000	U.S. EPA, 1978
		SALTWATER SPECIES			
Sheepshead minnow, *Cyprinodon variegatus*	1,2-dichloropropane	33 days	Growth inhibition	164,000	U.S. EPA, 1978

REFERENCES

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

Scott, C.R. and P.A. Wolf. 1962. The antibacterial activity of a series of quaternaries prepared from hexamethylenetetramine and halohydrocarbons. Appl. Microbiol. 10: 211.

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.

U.S. EPA. 1980. Unpublished laboratory data. Environmental Research Laboratory - Duluth.

Mammalian Toxicology and Human Health Effects

INTRODUCTION

For purposes of discussion in this document, "dichloropropane" refers to 1,2-dichloropropane and will be abbreviated "PDC" (for propylene dichloride); "dichloropropene" refers to 1,3-dichloropropene and will be abbreviated "DCP." In the case of the latter, the cis- or trans- isomer will be designated when known. Lack of such designation will indicate lack of further information on speciation or that a mixture of the two isomers is involved.

PDC and DCP are used primarily as soil fumigants, alone or in combination. PDC is also used as a solvent and a chemical intermediate, though comparative data concerning quantities utilized for pesticide and nonpesticide purposes were not found. D-D® is the Shell trademark for a combination preparation. The published analyses of this preparation vary, as seen in Table 1. Telone® is the Dow trademark for DCP. De Lorenzo, et al. (1977) described mutagenicity studies with Telone® containing 30 percent of each isomer of DCP and 20 percent DCP. Telone 2® described by Nater and Gooskens (1976) contains about 92 percent DCP and 3 to 5 percent PDC. PDC has also been marketed in combination with chlorpicrin; DCP has been marketed in combination with ethylene dibromide and carbon tetrachloride (Dowfume EB-5®).

Both PDC and DCP are volatile. The extent of this volatility is, as will be seen, an important consideration for interpretation of toxicological data and establishment of water quality criteria.

TABLE 1

Published Analytical Data on D-D® Soil Fumigant

	Composition (%)			
	Martin & Worthing (1974)	Spencer (1973)	De Lorenzo, et al. (1977)	Nater & Gooskens (1976)
1,3-Dichloropropene	nlt 50	60-66	40	53
cis-	+[a]	30-33	+	+
trans-	+	30-33	+	+
1,2-Dichloropropane	+	30-35	2	27
Other Chlorinated Hydrocarbons[b]	+	5		20

[a] +, present but quantity not indicated

[b] Other chlorinated hydrocarbons reported include one or more of: 3,3-dichloropropene; 2,3-dichloropropene; 1,2-dichloropropene; 2,2-dichloropropane; 1,2,3-trichloropropane; epichlorohydrin; allyl chloride.

Stanford Research Institute (1975), in a study for the National Science Foundation, reported that 60 million pounds per year of a mixture of DCP/PDC were produced for use as a soil fumigant. Thus, there is a potential for contamination of water and food via the soil.

EXPOSURE

Ingestion from Water

Dichloropropane and dichloropropene can enter the aquatic environment as discharges from industrial and manufacturing processes, as runoff from agricultural land, and from municipal effluents. These compounds have been identified but not quantified in New Orleans drinking water (Dowty, et al. 1975). The National Academy of Sciences' Safe Drinking Water Committee (1977) lists both PDC and DCP as organic contaminants found in finished drinking water, with no available information on chronic toxicity and with the highest concentration in finished water of 1.0 µg/l for each compound.

Ingestion from Food

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

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

When no measured steady-state bioconcentration factor (BCF) is available for any compound, the equation "Log BCF = (0.85 Log P) - 0.70" can be used (Veith, et al. 1979) to estimate the steady-state BCF for aquatic organisms that contain about 7.6 percent lipids (Veith, 1980) from the octanol/water partition coefficient (P). The measured log P value was obtained from Hansch and Leo (1979). When no measured value could be found, a calculated log P value was obtained using the method described in Hansch and Leo (1979). The adjustment factor of 3.0/7.6 = 0.395 is used to adjust the estimated BCF from the 7.6 percent lipids on which the equation is based to the 3.0 percent lipids that is the weighted average for consumed fish and shellfish in order to obtain the weighted average bioconcentration factor for the edible portion of all freshwater and estuarine aquatic organisms consumed by Americans (Table 2).

Inhalation

The atmospheric levels of PDC and DCP are not known. However, the possible sources of entry of these compounds to the atmosphere

TABLE 2

Estimated BCFs for Isomers of PDC and DCP

Compound	Log P Meas.	Log P Calc.	Estimated Steady State BCF	Weighted Average BCF
1,1-Dichloropropane		2.34	19.4	7.66
1,2-Dichloropropane		2.02	10.4	4.11
1,3-Dichloropropane	2.00		10	3.95
2,2-Dichloropropane		2.34	19.4	7.66
1,1-Dichloropropene		2.67	37.1	14.7
2,3-Dichloropropene		1.91	8.38	3.31
3,3-Dichloropropene		1.79	6.62	2.61
1,2-Dichloropropene (cis- and trans-)		2.07	11.5	4.54
1,3-Dichloropropene (cis- and trans-)		1.63	4.84	1.91

are from the manufacture of commercial fumigants, the production of oil and fat solvents, the agricultural use of fumigants, and from the use of PDC and DCP in drycleaning and degreasing processes. The exact amounts of PDC and DCP which each of the sources contribute to the atmosphere could not be ascertained.

Fumigant mixtures of PDC and DCP are applied to the soil in liquid form, usually by means of a chisel applicator. Small amounts of these mixtures escape into the atmosphere by natural diffusion up through the soil profile, and some may leak into the atmosphere from the soil surface through inadequately sealed chisel shank holes. An estimate of the total amount of cis-DCP lost to the atmosphere after a typical application of Telone® to a 30.5 cm depth in a warm, moist, sandy loam soil would amount to approximately 5 to 10 percent (Thomason and McKenry, 1973). The California State Department of Agriculture reported that in 1971 approximately 1,285 metric tons of pesticide containing DCP were used in that state. It can be estimated that approximately 72 tons, or 8 percent, of DCP were lost to the atmosphere (Calif. State Dep. Agric. 1971).

Since levels of PDC and DCP have not been measured in the atmosphere, it is impossible to determine the amounts of these compounds that could be inhaled by the general public. There appears to be an occupational risk to workers who handle these compounds, although information on actual exposure levels is not available in the published literature.

Dermal

Dermal exposure to PDC and DCP is of concern to people who must work with these compounds. This is especially true for the agricultural workers who must mix and apply these compounds to the fields.

PHARMACOKINETCS

No data were available which deal with the absorption, distribution, biotransformation, or elimination of PDC or DCP in humans. Only one report was found which deals with the pharmacokinetics of these compounds (Hutson, et al. 1971). This report deals primarily with the retention potential of the compounds; the presentation of data on which a pharmacokinetic model could be based is limited.

The investigators administered PDC and the cis- and trans-isomers of DCP to rats. For each of the compounds, six rats (200 to 250 g, Carworth Farm E strain) of each sex were dosed via stomach tube with 0.5 ml of arachis oil solution of 1,2-dichloro-(1-^{14}C)propane (0.88 mg, 8.5 µCi), cis-1,3-dichloro(2-^{14}C)propene (2.53 mg, 7.68 µCi), or trans-1,3-dichloro(2-^{14}C) propene (2.70 mg, 8.50 µCi). The excretion of radioactivity as percent of the administered dose was determined in the urine, feces, and expired air of these animals at 24-hour intervals over a 4-day period. The animals were sacrificed after the fourth day following the administration of the compounds, and the radioactivity remaining in their carcasses was measured.

Data resulting from the study are shown in Tables 3 and 4. The authors claim that 80 to 90 percent of administered radioactivity was eliminated within the first 24 hours. This would include the

TABLE 3

Rates of Excretion of Radioactivity from Rats After the Oral Administration of Three Components of D-D® *

Compounds	Sex	Excretion of radioactivity (% of administered dose) in 24-hr periods (after administration) 0-24	24-48	48-72	72-96	Total (0-96 hr)
				Urine		
1,2-Dichloropropane	M	48.5 ± 5.23	1.9 ± 0.45	0.5 ± 0.12	0.2 ± 0.03	51.1 ± 5.27
	F	51.9 ± 1.59	1.8 ± 0.22	0.4 ± 0.06	0.3 ± 0.05	54.4 ± 1.48
cis-1,3-Dichloropropene	M	81.3 ± 2.76	1.9 ± 0.21	0.6 ± 0.14	0.3 ± 0.06	84.1 ± 2.94
	F	80.3 ± 5.34	1.2 ± 0.29	0.4 ± 0.23	0.4 ± 0.23	82.3 ± 5.18
trans-1,3-Dichloropropene	M	54.6 ± 1.92	0.6 ± 0.06	0.3 ± 0.04	0.1 ± 0.02	55.6 ± 1.90
	F	58.7 ± 1.08	1.1 ± 0.16	0.5 ± 0.13	0.2 ± 0.09	60.5 ± 1.00
				Faeces		
1,2-Dichloropropane	M	5.0 ± 2.66	0.7 ± 0.10	0.9 ± 0.56	0.2 ± 0.08	6.8 ± 2.61
	F	3.8 ± 0.95	0.7 ± 0.12	0.2 ± 0.02	0.2 ± 0.02	4.9 ± 1.07
cis-1,3-Dichloropropene	M	2.0 ± 0.38	0.8 ± 0.28	0.3 ± 0.14	0.2 ± 0.08	3.3 ± 0.53
	F	1.4 ± 0.43	0.2 ± 0.04	0.1 ± 0.03	0.1 ± 0.05	1.8 ± 0.42
trans-1,3-Dichloropropene	M	1.3 ± 0.37	0.2 ± 0.11	0.4 ± 0.15	0.1 ± 0.05	2.0 ± 0.28
	F	1.9 ± 0.24	0.2 ± 0.10	0.2 ± 0.15	0.1 ± 0.02	2.4 ± 0.26

The values given are the means ±SEM for groups of six rats.

*Source: Hutson, et al. 1971.

TABLE 4

Recoveries of Radioactivity from Rats in the 4 Days Following Oral Administration of Three Components of D-D® *
(percent of administered dose)

Compounds	Sex	Recovery of radioactivity		Exhaled Air	
		Urine	Faeces	Carbon Dioxide**	Other volatile radioactivity**
1,2-Dichloropropane	M	51.1 ± 5.27	6.8 ± 2.61	----	----
	F	54.4 ± 1.48	4.9 ± 1.07	19.3 (5)	23.1 (5)
cis-1,3-Dichloropropene	M	84.1 ± 2.94	3.3 ± 0.53	5.3 (3)	----
	F	82.3 ± 5.18	1.8 ± 0.42	2.4 (3)	1.4 (2)
trans-1,3-Dichloropropene	M	55.6 ± 1.90	2.0 ± 0.28	22.7 (3)	----
	F	60.5 ± 1.00	2.4 ± 0.26	24.4 (3)	3.5 (2)

*Source: Hutson, et al. 1971.

**Values given are means for the numbers of animals indicated in parentheses. Except where indicated otherwise, values given are the means ±SEM for groups of six rats.

radioactivity in the expired air, though the data for that fraction for the first 24 hours were not given.

If 80 percent of the administered dose is eliminated in 24 hours, this would mean a total elimination constant of approximately 0.07 hr^{-1}. Approximately 50 percent of the administered dose of PDC and trans-DCP was eliminated by the urine in 24 hours. This would represent an elimination constant for urine of approximately 0.03 hr^{-1}. These compounds, on the basis of their physical properties, should distribute in total body water. In a rat a compound distributed in total body water with no accompanying storage or biotransformation would have a urinary elimination constant of approximately 0.50 hr^{-1}. Thus, the decreased clearance seen is due either to the renal tubular reabsorption (decreased clearance), incorporation into virtual volume of distribution (increased apparent volume of distribution), or both. The latter is the most likely, with compensation occurring by biotransformation. In the case of cis-DCP, the participation of biotransformation is more evident.

EFFECTS

Dichloropropane

Acute, Subacute, and Chronic Toxicity

The acute LD_{50} values which have been obtained for PDC and related compounds are shown in Table 5.

The earliest reference to the acute oral toxicity of the dichloropropanes in mammals was reported in a study of the anthelmintic action of orally administered dichloropropanes in dogs (Wright and Schaffer, 1932). An oral dose of 5,700 mg PDC per kg body weight caused loss of coordination and staggering 15 minutes

TABLE 5

List of LD_{50}s for Dichloropropane and Dichloropropene

Compound	Route	Species	LD_{50} Value	Notes	Reference
1,2-Dichloropropane	Inhalation	Rat	9224 mg/m^3	8 hr exposure - 3/6 mortality	Smyth, et al. 1969
	Oral	Rat	2200 mg/kg	Carworth-Wistar strain*	Smyth, et al. 1969
		Rat	2200 mg/kg	Russian Paper	Ekshtat, et al. 1975
		Guinea Pig	2000 to 4000 mg/kg	Lethal dose	Anon. 1967
	Dermal	Rabbit	10,200 mg/kg	Single dose skin penetration	Smyth, et al. 1969
1,1-Dichloropropane	Oral	Rat	6500 mg/kg	Carworth-Wistar strain*	Smyth, et al. 1954
	Dermal	Rabbit	16,400 mg/kg	Single dose skin penetration	Smyth, et al. 1954
1,3-Dichloropropene-1	Inhalation	Rat	4530 mg/m^3		Hine, et al. 1953
		Mice		Cumulative high acute toxicity	Hine, et al. 1953
	Oral	Rat	140 ± 25 mg/kg		Hine, et al. 1953
		Mice	300 ± 27 mg/kg		Hine, et al. 1953
	Dermal	Rabbit	2100 ± 260 mg/kg	Single dose skin penetration	Hine, et al. 1953
2,3-Dichloro-1-propene	Oral	Rat	320 mg/kg	Carworth-Wistar strain*	Smyth, et al. 1962
	Dermal	Rabbit	1930 mg/kg	Single dose skin penetration	Smyth, et al. 1962
D-D® (Nematocide)	Inhalation	Rat	4530 mg/kg	Long-Evans strain	Hine, et al. 1953
	Oral	Rat	140 ± 25 mg/kg	Long-Evans strain	Hine, et al. 1953
		Mice	300 ± 27 mg/kg	Long-Evans strain	Hine, et al. 1953
Telone® (Nematocide)	Oral	Rat male	713 mg/kg		Torkelson & Oyen, 1977
		Rat female	470 mg/kg		Torkelson & Oyen, 1977

*Single dose oral toxicity after 14 days.

after administration, complete lack of coordination after 90 minutes, followed by death 3½ hours after administration. An oral dose of 3,500 mg DCP per kg body weight caused staggering, partial narcosis, and death within 24 hours. The dogs killed by the oral administration of the dichloropropanes exhibited hypostatic congestion of the lungs, congestion of the kidneys and bladder, and hemorrhages in the stomach and respiratory tract. Pathologically the liver showed passive congestion and severe cloudy swelling, accumulation of large fat droplets in some lobules, and marked deposition of bile pigments around the central veins. The kidneys showed severe passive congestion and degeneration of the tubular epithelium. Oral doses as low as 350 mg of dichloropropane per kg body weight caused moderately severe lesions in the liver, gastrointestinal tract, and kidneys (Wright and Schaffer, 1932).

A series of inhalation toxicology studies by Heppel and his coworkers provide some information as to the relative toxicity of PDC. Initial studies (Heppel, et al. 1946) were done with rats, mice, guinea pigs, and rabbits (and dogs at 1,000 ppm) utilizing daily 7-hour exposure periods and a concentration range of 1,000 to 2,200 ppm. A concentration of 2,200 ppm was lethal to over 50 percent of the animals of all four species after up to eight exposures. Mice were the most sensitive, with 10 of 11 dying before the completion of one exposure period. In addition, animals were exposed to 1,600 ppm of PDC, but the data are no more revealing than that already presented.

Gross effects observed in the animals included weight loss, CNS depression (cortical and medullary), rales, and neuromuscular weakness. Prothrombin time, BSP excretion, total plasma protein, A/G ratio, BUN, and serum phosphate were not altered in the dogs which died after exposure to 1,000 ppm. Hematological studies indicated no changes except for "somewhat lower" red cell counts and hemoglobin in exposed rabbits.

Gross and histopathological examination revealed a range of liver abnormalities from visceral congestion to fatty degeneration to extensive multilobular areas of coagulation necrosis. Other pathological effects observed among animals from all concentrations included: renal tubular necrosis and fibrosis, splenic hemosiderosis, pulmonary congestion, bronchitis, pneumonia, and fatty degeneration in the heart. Subsequent studies utilizing 2,200 ppm were performed (Highman and Heppel, 1946) to obtain further pathological data. These studies served to further document the earlier observations.

In another inhalation study (Heppel, et al. 1948), rats, guinea pigs, and dogs were exposed to 400 ppm of PDC for 128 to 140 daily 7-hour periods (given five days per week). The only effect observed was a decreased weight gain by rats. However, considering the pharmacokinetic data discussed earlier, it may be that, by utilizing a five day per week schedule, the investigators were not attaining the prolonged exposure they might have anticipated.

Mice were then exposed in the same fashion. As in the previous study, mice (C57) were more sensitive to PDC, and apparent

treatment-related "slight fatty degeneration of the liver" was observed.

Sidorenko, et al. (1976) studied the effects of the continuous inhalation of 1 and 2 mg PDC/l air in albino male rats (200 to 400 g). Blood acetylcholinesterase and blood catalase activities, red and white blood cell counts, hemoglobin, and animal weight were measured after 2, 4, 24, 48, 72, and 96 hours, and after 6 and 7 days of continuous exposure. Histopathological examination of the liver and kidneys, determination of ribonocleic acid, glycogen, lipids, oxidation process (succinate dehydrogenase activity), DPN-diaphorase, acid and alkaline phosphatase, and quantitative evaluation of the liver DNA were performed on the exposed animals. Significant changes in catalase and cholinesterase activity and threshold index were observed as early as four hours after the start of the inhalation of 1.0 mg PDC/l. Significant changes occurred in all of the above mentioned tests after 24 hours of continuous exposure to 1.0 mg PDC/l air.

The livers of rats that were continuously exposed to 1.0 mg PDC/l air for seven days were examined histologically and showed protein and fat dystrophy, suppression of enzyme activity, and decreased ribonucleoproteins centralized in the centrolobular sections. Cells of peripheral sections of lobules showed fewer changes and underwent displacements of an adaptational nature in the form of hyperplasia and hypertrophy of cellular and intracellular structures. The number of unicellular polyploidal hepatocytes increased significantly, whereas the number of binuclear cells was reduced. In some instances the amount of ploidy equaled 16n.

These adaptive changes were accompanied by increased ribonucleoproteins and increased enzyme activity on the periphery of the hepatocytes. In the kidney, as in the liver, regions of greater or lesser sensitivity to PDC were found, and adaptational changes were found in the distal segments of the nephron which showed increased activity (Sidorenko, et al. 1976).

The effect of PDC on the functional state of the rat was further demonstrated by Kurysheva and Ekshtat (1975). Blood serum cholesterol, beta-lipoproteins, and gamma-globulin levels increased after the 10th day of daily oral doses of 14.4 and 360 mg PDC per kg body weight. By day 20 of dosing, the serum cholinesterase was inhibited, whereas the fructose-1-monophosphate aldolase, alanine transaminase, and asparagine transaminase were increased. After 30 days of dosing the alanine transaminase was inhibited.

In the range-finding studies of Smyth, et al. (1954, 1962, 1969), acute inhalation toxicity studies of new chemical compounds were performed to indicate the comparative hazards of handling these compounds and the degree of care necessary to protect the exposed workmen. The studies consisted of exposing groups of six male Carworth-Wistar rats (90 to 100 g body weight) to either saturated vapor or known vapor concentrations of compounds for a known period of time and then observing the mortality of the exposed rats during a 14-day observation period. It was recorded that a group of six rats could survive a 10-minute exposure in a saturated vapor atmosphere of PDC with no death during the 14-day observation period. In another exposure study, one 8-hour exposure to 2,000 ppm

PDC in air killed 3 of 6 rats during the 14-day observation period (Smyth, et al. 1969). It was found that a group of six rats could survive an exposure of only two minutes in a saturated vapor atmosphere of 1,1-dichloropropane (7,630 mg 1,1-dichloropropane/l air). One 4-hour exposure to 17.6 mg 1,1-dichloropropane/l air killed 4 of 6 rats within the 14-day observation period (Smyth, et al. 1954).

St. George (1937) described the effects of PDC poisoning in humans. Symptoms included headache, vertigo, lacrimation, and irritation of the mucous membrane. Changes in the blood are similar to those of "marked anemia."

Another case report described the acute oral toxicity of PDC in a 46-year-old man who accidently ingested about 50 ml of a cleaning solution containing PDC. Within two hours after ingestion, he went into a deep coma with mydriasis and hypertonia; after 24 hours he regained consciousness with treatment of artificial ventilation and osmotic diuresis. However, after 36 hours he went into irreversible shock and died of cardiac failure with lactic acidosis and hepatic cytolysis. Necropsy examination showed centro- and mediolobular acute hepatic necrosis (Larcan, et al. 1977).

Mutagenicity

De Lorenzo, et al. (1977) reported PDC to be mutagenic in *S. typhimurium* strains TA 1535 and TA 100 with or without metabolic conversion. No such activity was found in TA 1978, TA 1537, or TA 98 (Table 6). This implies missense, but not frameshift mutations. However, this is further discussed in the section dealing with mutagenicity of DCP.

TABLE 6

Mutagenicity of D-D®, Telone®, PDC and DCP as Determined by the "Ames" Test With (W) and Without (WO) Liver Microsomal Fraction*

		Number of mutant colonies/plate with Salmonella strains					
		TA 1978		TA 1535		TA 100	
Compound	Amount/plate	WO	W	WO	W	WO	W
Telone®	100 µg	24	115	12	15	178	151
	250 µg	36	225	48	59	225	191
	1 mg	45	249	75	90	263	242
	2.5 mg	53	270	115	135	425	385
	5 mg	61	365	150	220	282	500
	10 mg	15	150	78	61	192	212
D-D® soil fumigant	500 µg	11	123	35	42	125	112
	5 mg	38	181	45	61	198	250
	15 mg	80	300	151	151	350	450
	25 mg	75	446	145	150	470	512
cis-DCP	20 µg	19	21	243	77	594	731
	50 µg	90	71	680	490	1800	2100
	100 µg	119	131	1210	990	1750	1551
trans-DCP	20 µg	27	31	235	109	362	650
	50 µg	68	75	430	381	1750	2200
	100 µg	115	91	925	828	1820	1500
PDC	10 mg	27	38	75	81	220	185
	20 mg	38	21	210	185	480	450
	50 mg	48	15	411	312	850	920

*Source: De Lorenzo, et al. 1977.

Bignami, et al. (1977) also reported the mutagenicity of PDC in TA 1535 and TA 100. They studied the induction of point mutations (8-azaguanine resistance) and somatic segregation (crossing over and nondisjunction) in A. nidulans, using the spot test technique. PDC was shown to significantly raise the frequency of mutants resistant to 9-azaguanine.

Dragusanu and Goldstein (1975) reported that PDC causes chromosomal aberrations in rat bone marrow. Trace impurities of PDC were tested and found to be inactive.

Carcinogenicity

In none of the studies described to this point was evidence of carcinogenicity observed. However, Heppel, et al. (1948) tried to induce hepatomas in C3H strain of mice by repeated inhalation of 1.76 mg PDC/l air. Only 3 of 80 C3H strain mice survived a total of 37 exposure periods and a subsequent observation period of seven months, at which time the three remaining mice were 13 months of age. These three mice showed multiple hepatomas histologically similar to those induced by carbon tetrachloride. The livers of these mice also showed many large mononuclear cells laden with lipochrome resembling ceriod. Although inhalation of 1.76 mg PDC/l air induced hepatomas, too few mice survived the exposures and observation period to make a statistically valid evaluation. No hepatomas were observed in control animals.

Dichloropropene

Acute, Subacute, and Chronic Toxicity

Acute LD_{50}s for DCP and its isomers are given in Table 5. Most of the information on the toxicity of DCP comes from a study by Torkelson and Oyen (1977). Rats were exposed to 3 ppm (13.6 mg/m^3)

for periods of 0.5, 1, 2, or 4 hours/day, 5 days/week for 6 months. Only the rats exposed four hours per day showed an effect, and this was manifested as cloudy swelling of the tubular epithelium. Further studies were done on rats, guinea pigs, and rabbits exposed to 1 or 3 ppm of DCP, 7 hours per day for 125 to 130 days over a 180-day period. Hematological studies were run midway and near the end of the study. No changes which could be attributed to the treatment were seen in hematocrit, WBC, hemoglobin, or differential count. The only effects the authors described which could be attributed to treatment were cloudy swelling of renal tubular epithelium in male rats and an increase in liver weight/body weight ratio in female rats. Some rats were also allowed a 3-month recovery period. After this time no changes attributable to treatment were observed. In experiments preliminary to these (complete data not published), rats and guinea pigs were exposed to 50 ppm DCP, 7 hours per day for 19 out of 28 days and 27 out of 39 days. Changes attributable to treatment for the shorter period were equivocal. After the longer period, gross examination revealed some liver and kidney changes (Torkelson and Oyen, 1977). These authors also cited unpublished data of others indicating liver, kidney, and lung injury in animals receiving oral doses of DCP in the LD_{50} range. The studies of Torkelson and Oyen (1977) indicate 1 ppm DCP by inhalation as a no observable adverse effect level (NOAEL). The authors recommend this as a time-weighted threshold limit value (TLV).

Strusevich and Ekshtat (1974) investigated the effects of DCP on the trypsin, trypsin inhibitor, amylase, and lipase activities in the blood serum of albino rats. The animals were fed daily doses

of 0.1, 0.5, and 2.5 mg of DCP per kg body weight for six months. The results showed that the trypsin activity increased through the six months of administration, and the activity of trypsin inhibitor decreased after the second month of administration. The blood lipase activity permanently increased, and amylase tended to be reduced.

Kurysheva and Ekshtat (1975) studied the effects of daily oral doses of DCP on the functional state of the rat liver. They fed groups of albino rats daily oral doses of 2.2 and 55 mg of DCP per kg for 30 days. The results showed that by day 30 of administration the excretory liver function was altered, as evidenced by prolonged pigment circulation in the blood, raised thymol test values, cholesterol level, and stimulated increase of fructose 1-monophosphate aldolase.

In human sensory tests, 13.6 mg DCP/m^3 air was detected by 7 of 10 human volunteers who were exposed to 11.6 or 4.5 mg DCP/m^3 air for 1 to 3 minutes. Some of the volunteers reported fatiguing of the sense of smell after a few minutes of exposure. Seven of the ten volunteers were able to detect 4.5 mg DCP/m^3 air, but it was noticeably fainter (Torkelson and Oyen, 1977).

Mutagenicity

De Lorenzo, et al. (1977) reported that DCP was mutagenic to *S. typhimurium* TA 1535 and TA 100 but not the TA 1978, TA 1538, or TA 98. Mutagenicity was the same with or without the addition of liver microsomal fraction. The authors concluded that because the results are similar to those seen with PDC, the same mechanistic implications may exist.

In another study, Neudecker, et al. (1977) found the cis- and trans- isomers of DCP to give positive results in an assay system with strains TA 1535, TA 1537, and TA 1538. Both isomers of DCP were mutagenic to strain TA 1535 with and without microsomal activation. The cis- isomer was found to be two times more reactive than the trans- isomer.

Neudecker, et al. (1977) also found a significant difference in the survival rate of the bacteria exposed to varying concentration of both isomers. At all concentrations tested, survival rates of cells exposed to cis-DCP were generally lower than those of bacteria exposed to the trans- isomer.

It can be seen from Table 6 that DCP may be about three orders of magnitude more mutagenic than PDC. Also, it can be seen that Telone® and D-D® (see Table 1 for composition of the products used in this study) are mutagenic to TA 1535 and TA 100, as might be expected. However, they are also mutagenic to TA 1978 (in the presence of the microsomal fraction), indicating a frameshift mutation. In the Criterion Formulation section of this document it is suggested that mixtures of PDC and DCP may result in a negative deviation from Raoult's Law. That is, the vapor pressure of the mixture is lower than the vapor pressure of either individual component. The implication is that less evaporation of material may occur when the mixture is used. Another possibility is that the presence of one compound results in the forcing of the other through an alternate, or normally minor, metabolic pathway, leading to the formation of larger amounts of a normally minor mutagenic metabolite.

Carcinogenicity

Van Duuren, et al. (1979) designed a study to evaluate the carcinogenicity of 15 halogenated hydrocarbons by a multiple bioassay procedure. From their studies, the authors have suggested certain structure/activity relationships concerning carcinogenicity and the bioassay procedure. Among the compounds studied was cis-DCP. All studies utilized 30 male ICR/Ha Swiss mice per group. The compound was studied by three procedures.

(1) Initiation-Promotion: 122 mg applied once in 0.2 ml acetone followed 14 days later by 5 µg (in 0.2 ml acetone) of the tumor promoter, phorbol myristate acetate (PMA), three times weekly for 428 to 576 days.

(2) Repeated Skin Application: 41 or 122 mg in 0.2 ml acetone to shaved skin three times weekly for 400 to 494 days.

(3) Subcutaneous Injection: 3 mg in 0.05 ml trioctanoin injected subcutaneously in the left flank once weekly for 538 days.

In the initiator-promotor studies, six papillomas in four mice were observed. This result was not significantly different from promotor controls. Repeated skin application revealed three papillomas in three mice for the 122 mg dose; this was not significantly different from control animals which had no tumors. No tumors were observed for the animals receiving the 41 mg dose.

In the case of subcutaneous administration, six mice developed local sarcomas which represent a statistically significant difference relative to controls (0/100). In none of the studies were treatment-related remote tumors observed.

Dichloropropane/Dichloropropene
(mixtures containing at least 10 percent PDC)

Acute, Subacute, and Chronic Toxicity

Acute oral LD_{50} values for D-D® are shown in Table 5. Hine, et al. (1953) reported gross behavioral responses to lethal and near lethal doses similar to those seen for PDC and DCP alone. Gross pathological examination of the rats that died showed distention of the stomach by fluids and gas and erosion of the gastrointestinal mucosa, with occasional hemorrhage. Hemorrhage of the lungs and fatty degeneration of the liver were occasionally seen in rats that died several days after administration. The mortality curve was abrupt; all mice died at the highest dose level (432 mg D-D®/kg), about one-half at the next level (288 mg D-D®/kg), and only one at the two lowest levels (192 and 132 mg D-D®/kg body weight). Rats showed the same type of curve.

Hine, et al. (1953) also studied the acute inhalation toxicity of the commercial product D-D®. They exposed 24 adult Long-Evans strain rats for four hours to concentrations of D-D® ranging from 2,000 to 81,500 mg D-D®/m^3. The exposure to D-D ® caused respiratory distress, dyspnea, hypernea, mucous nasal discharge, and lacrimation. Dilatation of the capillaries was evident in the ears. Gross pathological examination of the rats that died from the exposures showed severe edema of the lungs, with varying degrees of interstitial and alveolar hemorrhage, and distention of the stomach and upper small intestine. Congestion and fatty degeneration of the liver also were noted occasionally in animals exposed to D-D®.

Russian scientists have investigated the effects of low oral and chronic doses of mixtures of dichloropropanes and dichloro-

propenes and D-D® in the exocrine function of the rat pancreas, the central nervous system, the kidney function in rabbits, and the functional state of the liver (Strusevich and Ekshtat, 1974, Fedyanina, et al. 1975; Kurysheva, 1974; Kurysheva and Ekshtat, 1975).

Strusevich and Ekshtat (1974) studied the effect of D-D® on the exocrine function of the pancreas by orally administering doses of 0.1, 0.6, and 3.0 mg D-D®/kg body weight to young male albino rats daily for six months. These doses of D-D® caused an increase in trypsin and lipase activities and decreased the trypsin inhibitor activity of the blood.

The percutaneous absorption of the product D-D® was studied by Hine, et al. (1953). Nineteen rabbits were depilated over the back and flanks in a cylindrical swath between the fore and hind legs, immobilized, and a tight-fitting girdle was slipped over the shaved area. Undiluted D-D® in doses of 1,200 and 4,800 mg/kg body weight were introduced under the girdle and was allowed to remain in contact with the skin for 24 hours. The rabbits exhibited decreased body movement and depressed respiration. One rabbit receiving 3,000 mg D-D®/kg had developed mucous nasal discharge. Seven of the ten rabbits receiving the three higher doses of D-D® died in 8 to 48 hours, and the five rabbits receiving the lowest dose (1200 mg D-D®/kg) survived.

Three cases of adverse reactions to D-D® have been reported in the Netherlands. Three patients had developed symptoms after several years of repeated exposures to the soil fumigant D-D® during its application to the fields. Most of the dermal contact

was through the feet, caused by the D-D® dripping inadvertantly into the shoes of the farmers during the spraying operation. By patch testing, the existence of a contact allergic sensitivity to D-D® could be proven in one patient. Patch tests with compounds related to D-D® suggest that the cause of contact allergy must be sought in the propene(s) fraction of D-D®. All three patients exhibited an itchy erythematous rash on the arms, face, and ears following contact with D-D® (Nater and Gooskens, 1976).

Mutagenicity

The mutagenicity of mixtures of PDC and DCP is discussed in the previous section.

Carcinogenicity

Pertinent data could not be located in the available literature concerning the carcinogenicity of mixtures of PDC and DCP.

CRITERION FORMULATION

Dichloropropane (PDC)

PDC has not been adequately tested for carcinogenicity, and chronic or subchronic ($<$ 90 days) oral toxicity data are not available. Based on either the TLV (ACGIH, 1977) or subchronic inhalation toxicity data (Heppel, et al. 1948), a pharmacokinetic model or the Stokinger and Woodward (1958) approach might be used to estimate an oral allowable daily intake (ADI) from which a water quality criterion could be derived; however, the subchronic inhalation data of Heppel and coworkers (1948) is somewhat ambiguous. Exposures to 400 ppm (1,867 mg/m^3), 7 hours per day for 128 to 140 days were noted to cause slight fatty degeneration of the liver in mice. However, under similar conditions, concentrations of 1,760 mg/m^3 caused high mortality in mice after 37 exposures. Consequently, the 1,867 mg/m^3 exposure cannot be used as a reasonable estimate of a lowest observable adverse effect level (LOAEL). Since the TLV is based primarily on the results of Heppel and coworkers (1948), the use of the TLV in deriving a criterion would not be appropriate. In addition, the positive mutagenicity studies on PDC have become available since the TLV was recommended.

The only other information that might be useful in assessing potentially hazardous levels of PDC in water is the study by Kurysheva and Ekshtat (1975), in which changes in serum enzyme levels were noted in rats after oral doses of 14.4 mg/kg/day for 30 days. Because of the short duration of this study, it cannot be used to derive a water quality criterion by the existing methodology. If a safety factor of 1,000 were applied to this lowest observable effect level (LOEL), the use of the standard assumptions

(70 kg human body weight, 0.0065 kg daily fish consumption, 2 l daily water consumption) and a bioconcentration factor of 4.11 results in a water level of 483 µg/l.

Dichloropropene (DCP)

DCP has not been adequately tested for carcinogenicity. When given to rats at daily oral doses of up to 2.5 mg/kg, DCP induced changes in blood serum enzymes after six months (Strusevich and Ekshtat, 1974). Daily oral doses of 2.2 and 55 mg/kg/day for 30 days caused changes in the liver function of rats (Kurysheva and Ekshtat, 1975). Taking the results of Strusevich and Ekshtat (1974), 2.5 mg/kg/day may be considered a LOEL for rats. However, the changes in liver function noted by Kurysheva and Ekshtat (1975) suggest that this may be near or at the LOAEL. Because of this uncertainty and because of the positive mutagenic activity of DCP in the absence of a valid test for carcinogenicity, a safety factor of 1,000 will be used to derive the ADI. Assuming a human body weight of 70 kg, the ADI is 175 ug (2.5 mg/kg/day x 70 kg - 1000). Given the bioconcentration factor of 1.91 and assuming a daily consumption of 2 l of water and 0.0065 kg of fish, the ambient water quality criterion (C) is 87 µg/l:

$$C = \frac{175\ \mu g}{2 + (0.0065 \times 1.91)} = 87\ \mu g/l.$$

A major problem with this criterion is that the DCP isomer or mixture of isomers used by Strusevich and Ekshtat (1974) was not specified. Although the available acute toxicity data (Table 5) do not suggest that the 1,3- and 2,3-isomers differ markedly, significant differences are apparent in the elimination rates of the cis-

and trans- forms of 1,3-dichloropropene. The inability to derive isomer-specific criteria, along with the previously discussed limitations of the general DCP criterion, should be considered in the use of this criterion.

Summary

A valid ambient water quality criterion for PDC cannot be derived. Based on the results of a 30-day oral study in rats, a water concentration of 483 µg/l can be calculated.

For DCP, an ambient water quality criterion of 87 µg/l can be calculated based on a six month oral study in rats. The criterion can be alternatively expressed as 14.1 mg/l if exposure is assumed to be from the consumption of fish and shellfish products alone.

REFERENCES

American Conference of Governmental Industrial Hygienists. 1977. Documentation of the Threshold Limit Values. 3rd. ed. Cincinnati, Ohio.

Anonymous. 1967. Hygenic guide series: Propylene dichloride. Am. Ind. Hyg. Assoc. Jour. 28: 294.

Bignami, M., et al. 1977. Relationship between chemical structure and mutagenic activity in some pesticides: The use of Salmonella typhimurium and Aspergillus nidulans. Mutag. Res. 46: 3.

California State Department of Agriculture. 1971. State pesticide use report.

De Lorenzo, F., et al. 1977. Mutagenicity of pesticides containing 1,3-dichloropropene. Cancer Res. 37: 1915.

Dowty, B., et al. 1975. Halogenated hydrocarbons in New Orleans drinking water and blood plasma. Science. 87: 75.

Dragusanu, S. and I. Goldstein. 1975. Structural and numerical changes of chromosomes in experimental intoxication with dichloropropane. Rev. Ig. Bacteriol. Virusol. Parazitol. Epidemiol. Pneumofitziol. Ig. 24: 37.

Ekshtat, B.Y., et al. 1975. Study of the cumulative properties of substances at different activity levels. Uch. Zap. Mosk. Nauchno. Isslend. Inst. G. 22: 46.

Fedyanina, W. Vn., et al. 1975. Comparative evaluation of methods to study the state of the central nervous system in studies on hygienic standardization. Gig. Savit. 3: 67.

Hansch, C. and A.J. Leo. 1979. Substituent Constants for Correlation Analysis in Chemistry and Biology. Wiley-Interscience, New York. p. 339

Heppel, L.A., et al. 1946. Toxicology of 1,2-dichloropropane (propylene dichloride). I. Studies on effects of daily inhalations. Jour. Ind. Hyg. Toxicol. 28: 1.

Heppel, L.A., et al. 1948. Toxicology of 1,2-dichloropropane (propylene dichloride). IV. Effect of repeated exposures to a low concentration of the vapor. Jour. Ind. Hyg. Toxicol. 30: 189.

Highman, B. and L.A. Heppel. 1946. Toxicology of 1,2-dichloropropane (proplyene dichloride). III. Pathologic changes produced by a short series of daily exposures. Arch. Pathol. 42: 525.

Hine, C.H., et al. 1953. Toxicology and safe handling of CBP-55 (technical 1-chloro-3-bromopropene-1). Am. Med. Assoc. Arch. Ind. Hyg. Occup. Med. 7: 118.

Hutson, D.H., et al. 1971. Excretion and retention of components of the soil fumigant D-D® and their metabolites in the rat. Food Cosmet. Toxicol. 9: 677.

Kurysheva, N.G. 1974. Some methodological problems of studying the functional state of the kidneys in a toxicological experiment. Uch. Zap. Mosk. Nauchno-Issled. Inst. Gig. 21: 126.

Kurysheva, N.G. and B.Y. Ekshtat. 1975. Effect of 1,3-dichloropropylene and 1,2-dichloropropane on the functional state of the liver in animal experiments. Uch. Zap. Mosk. Nauchno-Issled. Inst. Gig. 22: 89.

Larcan, A., et al. 1977. Acute poisoning induced by dichloropropane. Acta. Pharmacol. Toxicol. Suppl. 41: 330.

Martin, H. and C.R. Worthing. 1974. Pesticide Manual. 4th ed. Br. Crop Prot. Counc.

Nater, J.P. and V.H.J. Gooskens. 1976. Occupational dermatosis due to a soil fumigant. Contact Derm. 2: 4.

National Academy of Sciences. 1977. Drinking Water and Health. Safe Drinking Water Comm. Washington, D.C.

Neudecker, T., et al. 1977. *In vitro* mutagenicity of the soil nematocide, 1,3-dichloropropene. Experientia. 33: 8.

Sidorenko, G.I., et al. 1976. Methodological approaches to the study of the combined effect of atmospheric pollutants as illustrated by chlorinated hydrocarbons. Environ. Health Perspect. 13: 111.

Smyth, H.F., et al. 1954. Range-finding toxicity data: List V. Am. Med. Assoc. Arch. Ind. Hyg. Occup. Med. 10: 61.

Smyth, H.F., et al. 1962. Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. Jour. 23: 95.

Smyth, H.F., et al. 1969. Range-finding toxicity data: List VII. Am. Med. Assoc. Arch. Ind. Hyg. Occup. Med. 30: 470.

Spencer, H. 1973. Guide to chemicals used in crop protection. Agriculture Canada.

Stanford Research Institute. 1975. Unpublished data from files of Off. Water Pollut. Stand. U.S. Environ. Prot. Agency.

St. George, A.V. 1937. The pathology of the newer commercial solvents. Am. Jour. Clin. Pathol. 7: 69.

Stephan, C.E. 1980. Memorandum to J. Stara. U.S. EPA. July 3.

Stokinger, H.E. and R.L. Woodward. 1958. Toxicologic methods for establishing drinking water standards. Jour. Am. Water Works Assoc. 50: 515.

Strusevich, E.A. and B. Ekshtat. 1974. The effect of certain chlorinated hydrocarbons on the exocrine function of the pancreas. Gig. Savit. 1: 94.

Thomason, I.J. and M.V. McKenry. 1973. Movement and fate as affected by various conditions in several soils. Part I. Hallgardia. 42: 393.

Torkelson, R.R. and F. Oyen. 1977. The toxicity of 1,3-dichloropropene as determined by repeated exposure of laboratory animals. Jour. Am. Ind. Hyg. Assoc. 38: 217.

U.S. EPA. 1980. Seafood consumption data analysis. Stanford Research Institute International. Menlo Park, California. Final Report. Contract No. 68-01-3887.

Van Duuren, B.L., et al. 1979. Carcinogenicity of halogenated olefinic and alipahtic hydrocarbons in mice. Jour. Natl. Cancer Inst. 63: 1433.

Veith, G.D., et al. 1979. Measuring and estimating the bioconcentration factors of chemicals in fish. Jour. Fish Res. Board Can. 36: 1040.

Veith, G.D. 1980. Memorandum to C.E. Stephan. U.S. EPA. April 14.

Wright, W.H. and J.M. Schaffer. 1932. The anthelmintic action of propylene chloride in dogs. Am. Jour. Hyg. 16: 325.

☆ U S. GOVERNMENT PRINTING OFFICE 1980 720-016/4380