Integrated Laboratory Systems, Inc.

1,1-Dichloropropene
[563-58-6]

1,3-Dichloropropane
[142-28-9]

2,2-Dichloropropane
[594-20-7]

Final Review of Toxicological Literature

Prepared for

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EXECUTIVE SUMMARY

1,1-Dichloropropene, 1,3-dichloropropane, and 2,2-dichloropropane were nominated for review because these chemicals are candidates for drinking water regulations. All three chemicals are available from a number of U.S. suppliers, but production information was scarce. 1,3-Dichloropropane and 2,2-dichloropropane were produced in volumes of less than 1000 lbs. in 1977; no other production volume information was located.

No use information was located for 1,1-dichloropropene. 1,3-Dichloropropane is apparently used in production of other chemicals, with most source papers indicating its use in the production of cyclopropane. It was also frequently mentioned for use as a catalyst or initiator in polymerization reactions and as an organic solvent. 2,2-Dichloropropane has been used in the production of an isomerization catalyst and in the isomerization of saturated hydrocarbons.

Exposure to 1,3-dichloropropane may occur near industrial sites (by inhalation), from drinking water, and possibly from agricultural soils to which pesticide mixtures of 1,3-dichloropropene and 1,2-dichloropropane have been applied. 1,1-Dichloropropene, 1,3-dichloropropane, and 2,2-dichloropropane exposure may occur from working in production or handling facilities.

Based on secondary source information, 1,3-dichloropropane causes eye and skin irritation, and is moderately toxic by ingestion. No information was found on 1,1-dichloropropene or 2,2-dichloropropane. No human studies for any of the chemicals were located.

With regard to chemical disposition, metabolism, and toxicokinetics, very little information was located. 1,3-Dichloropropane was listed as a metabolite of 1,2,3-trichloropropane.

Mammalian acute toxicity values were located for 1,3-dichloropropane and 2,2-dichloropropane. Fourteen-day LD_{50}s for 1,3-dichloropropane by the oral route were 31.86 mmol/kg in mice and between 22.14 and 44.25 mmol/kg in rats; by intraperitoneal injection (i.p.), the LD_{50} was 7.08 mmol/kg in mice. The 24-hour LD_{50} for 1,3-dichloropropane in rats was 24.29 mmol/kg, when administered i.p. In rats, the dermal LD_{50} for 1,3-dichloropropane was greater than 17.70 mmol/kg and the inhalation LC_{50} was 0.32 mM. Acute oral toxicity effects of 1,3-dichloropropane included ulceration or bleeding of the stomach and small intestine (mice); piloerection, coma, and ataxia (rats); and chronic pulmonary edema, unspecified effects on the liver, and hemorrhaging (dogs). When administered i.p. to rats, 1,3-dichloropropane induced acute central nervous system effects. The lethal concentration (type not specified) of 2,2-dichloropropane by inhalation was less than 3500 ppm in rats.

Oral administration of 15.9 mmol 1,3-dichloropropane/day to rats induced languid behavior, salivation, tremors after dosing, and death within one week. A 5.31 mmol 1,3-dichloropropane/day oral dose for 14 days induced salivation in some rats, as well as significant increases in kidney and liver weights and significant decreases in testes/epididymis weights. In a

90-day study of the effects of oral 1,3-dichloropropane administration to rats, hepatic and renal toxicological effects were observed predominantly at a dose of 7.80 mmol/kg/day, but also to a lesser extent from doses of 0.44 and 1.77 mmol/kg/day. Short-term and subchronic exposure studies were not located for 1,1-dichloropropene and 2,2-dichloropropane.

No chronic exposure studies were located for any of the three chemicals.

In a two-year study evaluating the reproductive effects of 1,3-dichloropropane in mice given intermittent oral doses, the lowest effective dose was 1.15 mmol/kg, although the effects were not reported. Doses up to 3.54 mmol 1,3-dichloropropane/kg/day for 14 days did not induce effects on the male rat reproductive system. No studies reporting the reproductive toxicity or teratogenic effects of 1,1-dichloropropene or 2,2-dichloropropane were found.

No carcinogenicity studies were located for any of the three chemicals.

With regard to genotoxicity in prokaryotes, 1,1-dichloropropene was mutagenic in *Salmonella typhimurium* (strain and metabolic status not provided). 1,3-Dichloropropane was mutagenic in *S. typhimurium* strain TA1535 when tested with metabolic activation at concentrations of 4.43 mol/plate and higher. However, it was not mutagenic in strain TA1535 without metabolic activation or in strains TA98, TA 100, TA1537, TA1538 with or without metabolic activation when tested at concentrations up to 35.4 mol/plate. In another study, 1,3-dichloropropane was found to be mutagenic to strain TA100 at 10 mol/plate when tested without metabolic activation. 1,3-Dichloropropane was not mutagenic when tested in two *Escherichia coli* experiments, but was found to induce DNA damage in *Bacillus subtilis* when tested with, but not without, metabolic activation.

1,3-Dichloropropane did not induce aneuploidy (*Aspergillus nidulans*), chromosomal effects (*Saccharomyces cerevisiae*), or sex-linked recessive mutations (*Drosophila melanogaster*). 1,1-Dichloropropene and 2,2-dichloropropane also did not induce aneuploidy in *A. nidulans*.

In *in vitro* mammalian systems, 1,3-dichloropropane induced mutations (mouse lymphoma cells), sister chromatid exchanges (Chinese hamster V79 and ovary cells), DNA single-strand breaks and alkali-labile sites (human lymphocytes), and micronuclei (human lymphocytes). However, it did not induce chromosomal aberrations in rat liver RL4 cells. 1,3-Dichloropropane, administered as a single i.p. dose, did not induce micronucleated polychromatic erythrocytes in mice.

No immunotoxicity studies of the three chemicals were located.

In terms of structure-activity relationships, 1,1-dichloropropene, 1,3-dichloropropane, and 2,2-dichloropropane were evaluated against other chlorinated alkenes and alkanes. The chemicals did not possess the biophores, or structural components, found to induce mutagenicity or mitotic arrest and other cytotoxic effects.

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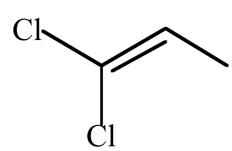
1.0 BASIS FOR NOMINATION

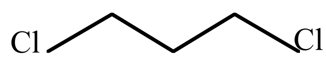
The EPA nominated 1,1-dichloropropene, 1,3-dichloropropane, and 2,2-dichloropropane for review since these chemicals are candidates for drinking water regulations. Public water works have required monitoring for these chemicals for about 15 years, although maximum exposure limits have not been set.

2.0 INTRODUCTION

1,1-Dichloropropene
[563-58-6]



1,3-Dichloropropane
[142-28-9]



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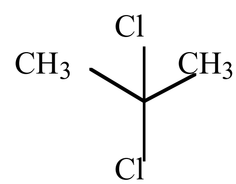
[594-20-7]



2.1 Chemical Identification

1,1-Dichloropropene ($C_3H_4Cl_2$; mol. wt. = 110.97) is also called:

1,1-Dichloropropylene

Propene, 1,1-dichloro-

1-Propene, 1,1-dichloro- (9CI)

1,3-Dichloropropane ($C_3H_6Cl_2$; mol. wt. = 112.99) is also called:

Trimethylene dichloride

Trimethylene chloride

2,2-Dichloropropane ($C_3H_6Cl_2$; mol. wt. = 112.99) is also called:

Propane, 2,2-dichloro- (8CI9CI)

Dimethyldichloromethane

Isopropropylidene chloride

2.2 Physical-Chemical Properties

2.2.1 1,1-Dichloropropene

1,1-dichloropropene has a thermal stability ranking of 81 on a scale of 1 (highest stability) to 320 (lowest stability) (Verschueren, 1996). No other physical-chemical property information was located.

2.2.2 1,3-Dichloropropane

Property	Information	Reference
Physical State	Clear, colorless liquid	CHRIS (2000)
Odor	Sweetish	CHRIS (2000)
Boiling Point (°C)	120.4	CHRIS (2000)
Melting Point (°C)	-99	Fisher (2000)
Flash Point (°C)	21	Fisher (2000)
Density (15 °C)	1.201	Lewis (2000)
Soluble in:	Water at 20 °C (0.8 g 1,3-dichloropropane/L water)	Fisher (2000)
	Water at 25 °C (2800 ppm)	EPA (1985)

1,3-Dichloropropane produces a flammable, irritating vapor (CHRIS, 2000). In fire, the chemical produces poisonous gases (CHRIS, 2000; Lewis, 2000). It is incompatible with oxidizing agents, acids, *o*-dichlorobenzene combined with ethylene dichloride, and aluminum (Fisher, 2000). Hazardous decomposition products include hydrogen chloride, phosgene, carbon monoxide, and carbon dioxide. 1,3-Dichloropropane has a thermal stability ranking of 165 on a scale of 1 (highest stability) to 320 (lowest stability) (Verschueren, 1996).

2.2.3 2,2-Dichloropropane

Property	Information	Reference
Physical State	liquid	Fisher (2000)
Boiling Point (°C)	69.3	EPA (1985)
Melting Point (°C)	33.8	EPA (1985)
Density (18 °C/4°C)	1.096	Lewis (2000)

2,2-Dichloropropane reacts explosively with dimethylzinc (Lewis, 2000) and is incompatible with strong oxidizing agents (Fisher, 2000). Hazardous decomposition products include hydrogen chloride, carbon monoxide, and carbon dioxide (Lewis, 2000; Fisher, 2000). 2,2-Dichloropropane has a thermal stability ranking of 224 on a scale of 1 (highest stability) to 320 (lowest stability) (Verschueren, 1996).

2.3 Commercial Availability

Most sources of 1,1-dichloropropene and 1,3- and 2,2-dichlopropanes supply high purity compounds, probably as analytical standards for use in monitoring drinking water supplies.

2.3.1 1,1-Dichloropropene

1,1-Dichloropropene is available in the U.S. from AccuStandard, Inc. (in high purity); Cresent Chemical Co.; Lancaster Synthesis, Inc.; Narchem Corp.; Pfaltz and Bauer, Inc.; Protocol Analytical Supplies, Inc. (in high purity); Sigma Chemical Co.; Supelco, Inc. (in high purity); and TCI America (Chem Sources, 2000).

No information on producers was located.

2.3.2 1,3-Dichloropropane

1,3-Dichloropropane is available in the U.S. from the following suppliers (Chemcyclopedia, 2000; Chem Sources, 2000):

Acros Organics USA;
Alfa Aesar (A Johnson Matthey Company) (in high purity);
Aldrich Chemical Co.;
AccuStandard, Inc. (in high purity);
Crescent Chemical Co.;
Creamova, Inc.;
ChemService, Inc. (in high purity);
Eastern Chemical Corp.;
Fisher Scientific Co.;
Fluka Chemical Co., Ltd.;

ICN Biomedicals, Inc.;
Narchem Corp.;
Pfaltz and Bauer, Inc.;
Protocol Analytical Supplies, Inc. (in high purity);
Sigma Chemical Co.;
Sithean Corp. (in bulk quantities, tank trunk and 55 gal. drums)[a];
SST Corp.
Supelco, Inc. (in high purity);
TCI America;
Wako Chemicals USA, Inc. (in high purity)
www.FOBChemicals.com

[a] Repeated attempts in August 2000 to contact Sithean Corporation were unsuccessful.

2.3.3 2,2-Dichloropropane

2,2-Dichloropropane is available in the U.S. from the following suppliers (Chemcyclopedia, 2000):

Aldrich Chemical Co.;
AccuStandard, Inc. (in high purity);
Crescent Chemical Co.;
ChemService, Inc. (in high purity);
Eastern Chemical Corp.;
Fluka Chemical Co., Ltd.;
Fluorochem USA;
ICN Biomedicals, Inc.;
Lancaster Synthesis, Inc.;
Pfaltz and Bauer, Inc.;
Protocol Analytical Supplies, Inc. (in high purity);
Sigma Chemical Co.; and
TCI America.

2,2-Dichloropropane is produced by Columbia Organics (EPA, 1985).

3.0 PRODUCTION PROCESSES AND ANALYSES

In the 1977 TSCA plant and producers survey, three manufacturers were listed: Eastman Kodak (no 1977 production), Columbia Organics (<1000 lb in 1977), and Shell Chemical (1 to 10 million pounds) (EPA, 1985)

1,3-Dichloropropane may be produced as a by-product by Dow Chemical USA, and Shell Chemical Co.in the commercial production of allyl chloride and dichloropropane-dichloropropene mixture (HSDB, 2000).

HSDB (2000) reported that 1,3-dichloropropane is probably produced by the high-temperature reaction of propylene with chlorine during the commercial production of allyl chloride and dichloropropene-dichloropropane mixtures.

1,3-Dichloropropane was obtained as a by-product in allyl chloride production involving propane chlorination in either the homogeneous (Costa Novella et al., 1983a) or heterogeneous phase (solid-phase catalyst) (Costa Novella et al., 1983b). A maximum yield of 36% 1,3-dichloropropane was found when prepared in the homogeneous phase and 41.5% in the heterogeneous phase. In these processes, 1,3-dichloropropane appears to be the by-product in the production of allyl chloride (Costa Novella et al., 1983b).

Reacting chloropropane (C_3H_7Cl) with carbon tetrachloride (CCl_4) and chlorine monoxide (Cl_2O) yields 43% 1,1-dichloropropane, 42% 1,2-dichloropropane, and 15% 1,3-dichloropropane (Wojtowicz, 1979).

Analytical methods for monitoring for 1,3-dichloropropane primarily include purge-and-trap analyses using gas chromatography/mass spectrometry (GC/MS) methods (HSDB, 2000). EPA Methods 502.1, 502.2, 524.1, 524.2, 1624, and 8260 provide guidance on specific techniques.

No production process or analysis information was located for 1,1-dichloropropene or 2,2-dichloropropane.

4.0 PRODUCTION AND IMPORT VOLUMES

In 1977, Columbia Organics produced less than 1000 lbs. of 1,3-dichloropropane and Shell Chemical produced between one and ten million lb (EPA, 1985). During that year, Columbia Organics also produced less than 1000 lb. of 2,2-dichloropropane. No information was located for 1,1-dichloropropene.

5.0 USES

No use information was located for 1,1-dichloropropene.

Tentative commercial uses for 1,3-dichloropropane based largely on patents are shown in **Table 1**.

1,3-Dichloropropane has been patented or recommended for use as a solvent or polymer swelling agent (at least 7 patents or articles; e.g., use as the solvent in the bromination of biphenyl to produce 4,4′-dibromobiphenyl [Okisaki et al., 1989]); in the composition of polymerization catalysts (usually Ziegler-Natta catalysts for polyolefin production, e.g., polyethylene and polypropylene) (8 references; e.g., see those in Table 1); as a reactant for branching or crosslinking polymers (3 references; e.g., Shaw, 1992; patent assignee Phillips Petroleum Co., USA); and dye synthesis (2 references; e.g., an indicator dye to determine lithium in blood [Delton and Eiff, 1989; patent assignee Eastman Kodak USA]). Other proposed uses (12 references) include production of cyclopropane (see references in Table 1), insulating oil (Wiegner and Schnurpfeil, 1998), a quaternized surfactant (Cretu et al., 1982), and tetrachloropropenes (Boyce, 1997; patent assignee LaRoche Industries, USA) and use as a corrosion inhibitor in reactor vessels for vinyl chloride polymerization (Tadasa and Kakitani, 1979; patent assignee Mitsubishi Monsanto). Phillips Petroleum Co., USA (Kubicek and Wu, 1994), has also patented the use of 1,3-dichloropropane, among many other chlorinated hydrocarbons, in the production of an organoaluminum isomerization catalyst for C4-C8 hydrocarbons. Dow Chemical Co., USA (Dow Chemical Co., 1965, 1966; Wilson, 1969) patented the use of dihaloalkanes, including 1,3-dichloropropane as a catalyst or initiator for production of polyalkyleneimines (polyaziridines) in aqueous solution.

Although occasionally mentioned in database records as a soil fumigant, presumably due to typographical or translator errors, 1,3-dichloropropane is not and has never been a registered pesticide in the United States. It has not been reported as a constituent of the commercial dichloropropane and dichloropropene mixtures, which are predominantly 1,2-dichloropropane (propylene chloride) and 1,3-dichloropropene (OHMTADS, 1985). However, it has been found in the soil after application of such nematocide mixtures. An abstract of one Japanese patent was found that claimed 1,3-dichloropropane for use as a soil insecticide or nematocide (Hokko Chemical Industry Co., Ltd., Japan, 1985). The only other agricultural use found in *Chemical Abstracts* was in a preservative for cut flowers.

2,2-Dichloropropane may be used in the production of an isomerization catalyst and in the isomerization of saturated hydrocarbons (Kubicek and Wu, 1994).

Table 1. Uses for 1,3-Dichloropropane.

Use	Reference
In the production of cyclopropane (an anesthetic), where 1,3-dichloropropane undergoes cyclization in the presence of zinc and sodium iodide. Patents have stated this method is a rapid and inexpensive technique.	Gluesenkamp (1937); Hass and Hass and Hinds (1937; 1941a,b); Ort (1941a,b); Mazac (1981); Budavari (1996)
As a component of Ziegler-Natta catalysts in the polymerization of olefins, especially propylene and ethylene	Kondo et al. (1987); Masi et al. (1994), Mitsui Toatsu Chem. (1985); Bujadoux et al. (1992); Tashiro and Yokoyama (1973); Benton et al. (1981)
As a catalyst or initiator in the production of polyalkyleneimines (polyaziridines) such as polyethyleneimine	Wilson (1969), Dow Chemical Co. (1965; 1966); Bembitskii et al. (1972)
In conjunction with a solid acidic catalyst for formaldehyde trimerization to *s*-trioxane.	Asakawa and Narita (1970)
As a coupling agent for block copolymers in the production of hot-melt adhesives.	Iio et al. (1986)
In the etherification of hydroxybenzophenone.	Kakuchi et al. (1992)
As an organic solvent for: • biphenyl bromination • dissolution of cellulose in the presence of amines and sulfur dioxide • recrystallization for purification of the pharmaceutical nefazodone.	Okisaki et al. (1989) Yamazaki et al. (1974) Artus Surroca (2000)

Table 1. Uses for 1,3-Dichloropropane (Continued).

Use	Reference
As an alkylating agent.	EPA (1985); Raabe et al. (1989); Wiegner and Schnurpfeil (1998)
In the production of dihydroxy *bis*-sulfides.	Shaw (1992)
As a lithium battery cathode (U.S. Navy research reports)	Smith et al. (1984; 1989a; 1989b)
As a swelling agent for styrene copolymer beads before or during sulfonation in the production of a cation-exchange resin.	Srejber (1983,
With a sulfide compound as a corrosion inhibitor for reactor vessels for vinyl chloride polymerization.	Tadasa and Kakitani (1979,
In a high-temperature chlorination process for the preparation of polychloroolefins, specifically tetrachloropropenes	Boyce (1997)
In the preparation of quaternary ammonium salts.	Cretu et al. (1982)
As a soil insecticide and nematocide.	Hokko Chem. Ind. (1985)
In a condensation step during the preparation of: • azo dyes • tetrasubstituted aryl cyclic formazan indicator dyes	Schleusener (1983) Delton and Eiff (1989)
As a solvent in the preparation of adiponitrile to prevent $(NCCH_2CH_2)_2O$ formation during the process.	Hasiguchi and Kamada (1971)
In the synthesis of end-functional polymers to form the halide end group.	Hirao et al. (1997)

6.0 ENVIRONMENTAL OCCURRENCE AND PERSISTENCE

6.1 Air

1,3-Dichloropropane was detected in the air surrounding a brominated chemical plant in Arkansas (EPA, 1985). The concentration was not provided. Around other industrial sites, 1,3-dichloropropane has been detected at levels of 2 ppb in ambient air.

If 1,3-dichloropropane were released into the air, it would disperse and degrade primarily by reaction with photochemically produced hydroxyl radicals (HSDB, 2000). In the air, 1,3-dichloropropane has a half-life of 9.5 days. It would also be washed out by rain.

When exposed to radiation of wavelength less than 290 nm, 1,3-dichloropropane undergoes photolysis, although this response is listed as not environmentally important (EPA, 1985).

In an EPA-funded experiment evaluating the pathways and products involved in incomplete incineration by hazardous waste incinerators, 1,3-dichloropropane and 2,2-dichloropropane were found to undergo dehydrochlorination during incineration, forming chloropropene (Dellinger et al., 1988).

The incineration temperature for 99% destruction of 1,1-dichloropropene at 2.0-second residence time under oxygen-starved reaction conditions is 780 ^{o}C (Verschueren, 1996).

6.2 Water and Soil

1,3-Dichloropropane was identified in only 68 of 14,101 drinking water samples tested in California between 1984 and 1998 (CA Dept. of Health, 2000), and has also been identified at concentrations up to 0.8 ppm in water from the Ohio River and its tributaries (EPA, 1985). However, 1,1-dichloropropene, 1,3-dichloropropane, and 2,2-dichloropropane were among chemicals monitored, but not detected, in the ground and surface waters of the San Joaquin-Tulare Basins in California (USGS, 1998).

If released into the soil or water during production and/or use, 1,3-dichloropropane would be lost primarily by volatilization (EPA, 1985; HSDB, 2000). A half-life of four hours was calculated for a model river. In another study, 1,3-dichloropropane had an environmental hydrolysis half-life of 2.2 years at 25 ^{o}C and pH 7 (Verschueren, 1996). The compound is poorly adsorbed by soil and has the potential for leaching. Bioconcentration in fish would not be significant (EPA, 1985; HSDB, 2000).

In a five-day experiment evaluating the biodegradability of 1,3-dichloropropane using filtered effluent from a wastewater treatment plant, the theoretical biological and chemical oxygen demands were 17 and 74%, respectively (EPA, 1985).

2,2-Dichloropropane has an environmental hydrolysis half-life of 1.46 days at 25 ^{o}C and pH 7 (Verschueren, 1996).

An experiment was conducted to evaluate the leaching behavior of the soil fumigants Telone I and Telone II, which contain 1,3-dichloropropane as a trace contaminant (<0.1% and <<0.1% by weight, respectively) (Zebarth and Szeto, 1999). After application of Telone and

Telone II to a packed soil column, more 1,3-dichloropropane was recovered in leachate (mean: 147.5 ± 7.68 µg and 21.7 ± 1.10 µg, respectively) than remained in soil (mean: 5.02 ± 1.10 µg and 1.63 ± 0.13 µg, respectively). Assuming a 1,3-dichloropropane concentration of 0.1% in Telone, the authors estimated that recovery of 1,3-dichloropropane was 34% after the Telone treatment. The other compounds in Telone and Telone II (1,3-dichloropropene, 1,2-dichloropropane, 2,3-dichloropropene, 1,2,2-trichloropropane, and 1,2,3-trichloropropane) were relatively persistent in soil, with up to 18.1% percent of each compound being recovered in leachate and 11.4% remaining in soil. Based on the amount recovered, the authors felt that 1,3-dichloropropane was at least as persistent as the other chlorinated hydrocarbons studied.

1,3-Dichloropropane was not detected in sampling of the leachate from five municipal landfills, nine non-municipal landfills, and six hazardous substance landfills (EPA, 2000).

7.0 HUMAN EXPOSURE

Based on its occasional occurrence in water well samples (CA Dept. of Health, 2000), exposure to 1,3-dichloropropane may occur from drinking water.

Exposure may also occur from working in 1,1-dichloropropene, 1,3-dichloropropane, and/or 2,2-dichloropropane production or handling facilities.

8.0 REGULATORY STATUS

1,1-Dichloropropene, 1,3-dichloropropane, and 2,2-dichloropropane were included on the EPA Drinking Water Contaminant Chemical List (EPA, 1998a). This list is required under the 1996 Safe Drinking Water Act Amendments and includes chemicals that are not subject to any proposed or promulgated national primary drinking water regulation and that are anticipated to occur in public water systems. The purpose is to identify chemicals that may require regulations under Section 1412(b)(1) of the SDWA. 2,2-Dichloropropane was cited as a chemical with prioritization for regulatory determination, while 1,1-dichloropropene and 1,3-dichloropropane were slated as research priorities.

Under 40 CFR Parts 141 and 142, 1,1-dichloropropene, 1,3-dichloropropane, and 2,2-dichloropropane are unregulated contaminants that must be monitored in all community water systems, although maximum contaminant levels (MCLs) have not been established (EPA, 1987). As of December 31, 1998, this requirement has been suspended for small public water systems (i.e., those serving 10,000 or less persons) in an effort to save money; monitoring of these water systems is still required under the 1996 Safe Drinking Water Act Amendments (EPA, 1999), as mentioned above. Under the EPA National Primary Drinking Water Regulations (NPDWRs), 1,3-dichloropropane and 2,2-dichloropropane are listed as unregulated contaminants (EPA, 2000).

According to the 1991 CERCLA Reportable Quantities Regulations (40 CFR 302.4), persons in charge of vessels or facilities are required to notify the National Response Center immediately when there is a release of 1000 lb (454 kg) or more of 1,3-dichloropropane (HSDB, 2000).

As of 1991 regulations, Section 8(d) of TSCA (40 CFR 716.20) requires manufacturers, importers, and processors of 1,3-dichloropropane to submit copies of unpublished health and safety studies to EPA (HSDB, 2000). Similarly, Section 8(a) of the rule (40 CFR 712.30) requires manufacturers of 1,3-dichloropropane to report to EPA preliminary assessment information concerned with production, use, and exposure, as stated in the preamble of 51 FR 41329.

With regard to packaging and handling, both 1,3-dichloropropane and 2,2-dichloropropane are categorized as flammable liquids (Fisher, 2000). 1,3-Dichloropropane is regulated and labeled as a UN Hazard Class 3, UN Subsidiary Risks 6.1, and UN Packing Group II material (WHO/IPCS/ILO, 1993). 2,2-Dichloropropane is regulated and labeled as a UN Hazard Class 3.2 and UN Packing Group II material (Fisher, 2000).

The State of California has included 1,3-dichloropropane in its list of chemicals to be evaluated in an effort to set legally enforceable maximum contaminant levels for compounds in drinking water that pose potential danger to human health (Brown et al., 1990). However, as of the 2000 California Drinking Water Standards, the compound is listed as an unregulated chemical requiring monitoring (22 CCR Sec. 64450) (CA Dept. of Health Services, 2000).

9.0 TOXICOLOGICAL DATA

9.1 General Toxicology

The MSDS for 1,3-dichloropropane lists it as an eye, skin, and respiratory irritant (Fisher, 2000). In *Sax s Dangerous Properties of Industrial Materials*, 1,3-dichloropropane is listed as moderately toxic by ingestion (Lewis, 2000).

9.1.1 Human Data

1,3-Dichloropropane vapors may cause a smarting of the eyes and respiratory system in high concentrations, although this effect is temporary (HSDB, 2000). Prolonged dermal exposure may cause smarting and reddening of the skin. 1,3-Dichloropropane has also been found to alter pancreatic function, as a late effect.

9.1.2 Chemical Disposition, Metabolism, and Toxicokinetics

1,3-Dichloropropane is a metabolite of 1,2,3-trichloropropane (Weber and Snipes, 1992; cited by Doherty et al., 1996). No additional information was located.

9.1.3 Acute Exposure

Acute toxicity values for 1,3-dichloropropane in mammals are presented in **Table 2**. Although acute toxicity information in aquatic species is not typically included, it was included here (**Table 3**) since it is thought that exposure may occur from water sources, and because of the scarcity of mammalian information. Additional acute toxicity information is provided in **Table 4**.

Table 2. Acute Toxicity Values for 1,3-Dichloropropane (in Mammals)

Route	Species (sex and strain)	LD_{50}/LC_{50}	Reference
oral	Mice (sex and strain n.p.)	3600 mg/kg (31.86 mmol/kg)	Terrill et al. (1991)
oral	Rats (M and F, Wistar)	Between 1250 and 2500 mg/kg (22.14 and 44.25 mmol/kg)	Shell Oil Co. (1979b)
i.p.	Mice (M and F, Crl: CD-1 [ICR] Br)	800 mg/kg (7.08 mmol/kg)	Crebelli et al. (1999)
i.p.	Rats (M, Long-Evans)	2744 mg/kg (24.29 mmol/kg)*	Herr and Boyes (1997)
dermal	Rats (M and F, Wistar)	>2000 mg/kg (>17.70 mmol/kg)	Shell Oil Co. (1979)
inhalation	Rats (M and F, Wistar)	36 mg/L (0.32 mM)	Shell Oil Co. (1982)

*24-hour LD_{50}
Abbreviations: F = female; i.p. = intraperitoneal; LC_{50} = concentration lethal to 50% of test animals; LD_{50} = dose lethal to 50% of test animals; M= male; n.p. = not provided

Table 3. Acute Toxicity Values for 1,3-Dichloropropane (in Aquatic Species)

Species	Length of Exposure	LC_{50}	Reference
Algae (*Scenedesmus subspicata*)	72 h	221 ppm (1.96 M)*	Freitag et al. (1994)
Daphnids (*Daphnia magna*)	24 h	39 ppm (0.35 M)*	Freitag et al. (1994)
Daphnids (*Daphnia magna*)	48 h	28,000 g/L (0.24 mM)	OHMTADS (1982)
Goldfish (*Carassius auratus*)	24 h	160,000 g/L (1.42 mM)	OHMTADS (1982)
Guppy (*Poecilia reticulata*)	7 d	84 mg/L (0.74 mM)	Verschueren (1996)
Menidia beryllina	96 h	10 mg/L (88.5 M)	Verschueren (1996)
Microorganisms of activated sludge	5 d	731 ppm (6.47 M)*	Freitag et al. (1994)

Table 3. Acute Toxicity Values for 1,3-Dichloropropane (in Aquatic Species) (Continued)

Species	Length of Exposure	LC_{50}	Reference
Mysidopsis bahia	96 h	10,300 g/L (91.2 M)	EPA (1980)
Photobacteria (*Photobacterium phosphoreum*)	15 min	152 ppm (1.35 M)*	Freitag et al. (1994)
Pimephales promelas	24 h	130 mg/L (1.15 mM)	Verschueren (1996)
Pimephales promelas	96 h	131 mg/L (1.16 mM)	Verschueren (1996)

*Reported as an EC_{50}, which is the effective concentration that is toxic to 50% of the test species.
Abbreviations: d = days; h = hours; LC_{50} = concentration lethal to 50% of test animals; min = minutes; ppm = parts per million

9.1.3.1 Oral Administration

Acute oral toxicity effects of 1,3-dichloropropane in mice include ulceration or bleeding of the stomach and small intestine (RTECS, 1982). Symptoms observed in rats included piloerection (at 11.06 mmol/kg) and coma and ataxia (at doses of 22.14 or 44.25 mmol/kg) (Shell Oil Co.; 1979b). Dogs experienced chronic pulmonary edema, unspecified effects on the liver, and hemorrhaging in a study reporting the LD_{LO} as 27 mmol/kg (RTECS, 1932).

9.1.3.2 Intraperitoneal Administration

Herr and Boyes (1991) reported, based on an i.p. study using rats, that organic solvents (including 1,3-dichloropropane) may have multiple acute central nervous system effects that are not predictable solely based on the lipid solubility of the compound; 1,3-dichloropropane produced significant changes in the latency and amplitude of multiple components of flash-evoked potential waveforms.

An i.p. LD_{LO} of 26.55 mmol 1,3-dichloropropane/kg was reported in dogs (Lewis, 2000).

Table 4. Acute Exposure to 1,3-Dichloropropane or 2,2-Dichloropropane

Species (Strain and Age)	Number and Sex of Animals	Chemical Form and Purity	Dose and Route	Exposure/ Observation Period	Results/Comments	Reference
9.1.3.1 Oral Administration						
Mice (strain and age n.p.)	n.p.	1,3-dichloropropane, purity n.p.	Presumed oral administration; dose and route n.p.	Single exposure; observation period n.p.	LD_{50} = 3600 mg/kg (31.86 mmol/kg) Induced ulceration or bleeding of the stomach and small intestine.	RTECS (1982)
Rats (Wistar, age n.p.)	4 M and 4 F per dose group	1,3-dichloropropane, purity n.p.	1250, 2500, or 5000 mg/kg (11.06, 22.14, or 44.25 mmol/kg) by gavage	Single exposure; observed for 14 days	Mortality rates were 0/8, 6/8, and 8/8, respectively for the three dose groups. Death occurred between days 2 and 4. The LD induced piloerection and lethargy. The rats recovered by day 3, and gained weight over the observation period. The MD and HD induced coma and ataxia. Of the two surviving rats given the MD, one became ataxic on day 2 and recovered and the other recovered from coma by day 4.	Shell Oil Co. (1979b)
Dogs (strain and age n.p.)	n.p.	1,3-dichloropropane, purity n.p.	Oral, dose n.p.	Single exposure; observation period n.p.	LD_{LO} = 3 g/kg (27 mmol/kg) Induced chronic pulmonary edema, unspecified effects on the liver, and hemorrhaging.	RTECS (1932)
9.1.3.2 Intraperitoneal Administration						
Rats (Long-Evans, 60 to 90-days-old)	18-20 M per dose group	1,3-dichloropropane, purity n.p.	0, 86, 172, 343, or 686 mg/kg (0, 0.76, 1.52, 3.04, or 6.07 mmol/kg) i.p.	Single exposure; Observed before dosing (to establish baseline) and then 0.5, 1,4, and 24 h after treatment.	Produced significant changes in latency and amplitude of multiple components of flash-evoked potential waveforms (i.e., reduced peaks N_{30} and N_{160}). The authors concluded that organic solvents may have multiple acute central nervous system effects that are not predictable solely based on the lipid solubility of the compound.	Herr and Boyes (1991)

Table 4. Acute Exposure to 1,3-Dichloropropane or 2,2-Dichloropropane (Continued)

Species (Strain and Age)	Number and Sex of Animals	Chemical Form and Purity	Dose and Route	Exposure/ Observation Period	Results/Comments	Reference
Dogs (strain and age n.p.)	n.p.	1,3-dichloropropane, purity n.p.	i.p; dose n.p.	Single exposure; observation period n.p.	LD_{Lo} = 3000 mg/kg (26.55 mmol/kg) Additional information n.p.	Lewis (2000)
9.1.3.3 Inhalation Exposure						
Rats (strain and age n.p.)	n.p.	2,2-dichloropropane, purity n.p.	Administered by inhalation; dose n.p.	Single 6 h exposure; observation period n.p.	Lethal concentration was reported as >3500 ppm (143 mmol/m^3). Ptosis was induced at that dose.	RTECS (2000)

Abbreviations: F = female(s); h = hour(s); HD = high dose; i.p. = intraperitoneal(ly); LD = low dose; LD_{Lo} = lowest lethal dose; M = male(s); MD = mid-dose; n.p. = not provided

9.1.3.3 Inhalation Exposure

An inhalation lethal concentration of less than 3500 ppm 2,2-dichloropropane was reported for rats (RTECS, 2000), although it was not specified whether this was an LC_{50} or the result of testing with only one or a few animals where such a dose could not be calculated.

9.1.4 Short-Term and Subchronic Exposure

The details of these studies are presented in **Table 5**.

Daily oral administration of 15.9 mmol 1,3-dichloropropane to rats induced languid behavior, salivation, tremors after dosing, and death within one week (Terrill et al., 1991). A 5.31 mmol/day oral dose for 14 days did not induce death, but caused salivation in some of the rats; significant increases in kidney weights (males only) and liver weights (males and females), as well as a decrease in the percent body weight of the testes/epididymis, were observed.

In a 90-day study of the effects of oral 1,3-dichloropropane administration to rats, hepatic and renal toxicity were induced at a dose of 7.08 mmol/kg/day (Terrill et al., 1991). A 1.77 mmol/kg/day dose induced only minimal treatment-related effects on the liver and kidney, and a 0.44 mmol/kg/day dose induced increased liver weight in females. The only toxic sign observed throughout treatment was urine-stained fur in one female administered 7.08 mmol/kg/day.

9.1.5 Chronic Exposure

No chronic exposure studies of 1,1-dichloropropene, 1,3-dichloropropane, or 2,2-dichloropropane were located.

Table 5. Short-term and Subchronic Exposure to 1,3-Dichloropropane

Species, Strain, and Age	Number and Sex of Animals	Chemical Form and Purity	Route, Dose, and Duration	Observation Period	Results/Comments	Reference
Rats (CD, 42-days-old)	10 M and 10 F per dose group	1,3-dichloropropane, 100% pure	0, 200, 600, or 1800 mg/kg/day (0, 1.77, 5.31, or 15.9 mmol/kg /day) by gavage for 14 days	Sacrificed the day after the final dose; observed throughout treatment period.	All animals in the HD group died before the end of week 1. Toxic signs included languid behavior, salivation, and tremors after dosing. Some of the rats in the MD group also experienced salivation. No treatment-related differences in body weight, food consumption, or hematology data were observed in the LD and MD groups. In M from the MD group, kidney and liver weights (actual and percent body weight) were significantly increased, and percent body weight (but not actual weight) of the testes/epididymis was significantly decreased. F in this dose group had significantly elevated liver weights as determined by actual weight and percent body weight. F experienced significant increases total protein (LD and MD) and albumin (MD) in blood. M in the MD group experienced significant increases in potassium and decreases in blood urea nitrogen. Urine pH was significantly decreased in M in the LD and MD groups and in F in the MD group.	Terrill et al. (1991)

Table 5. Short-term and Subchronic Exposure to 1,3-Dichloropropane (Continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form and Purity	Route, Dose, and Duration	Observation Period	Results/Comments	Reference
Rats (CD, 42-days-old)	10 M and 10 F per dose group	1,3-dichloropropane, 100% pure	0, 50, 200, and 800 mg/kg/day (0, 0.44, 1.77, and 7.08 mmol/kg/day) by gavage for 90 days	Sacrificed the day after the final dose; observed throughout treatment period.	One rat died during the course of the study, but the death was not considered to be treatment-related. The only toxic sign observed was urine-stained fur in F administered the HD. Centrilobular hepatocellular hypertrophy was observed in 1/10 F in the MD group, and in 9/10 F and 10/10 M in the HD group. Chronic progressive nephropathy was observed in 1/10 F in the LD group, 3/10 M in the MD group, and 7/10 M and 3/10 F in the HD group. Significant increases were observed in the following: • serum alkaline phosphatase (M and F at HD); • serum alanine aminotransferase (M at HD); • serum protein (F at MD); • serum albumin (M and F at MD, M at HD); • absolute liver weight (F at LD; M and F at MD and HD); • relative liver weight (M and F at MD and HD); • absolute kidney weight (F at MD, M and F at HD); and • relative kidney weight (M and F at HD). Terminal body weight was significantly decreased in M at the HD. The authors concluded that hepatic and renal toxicologic effects were induced at the HD, and that the minimal effects on the liver and kidney at the MD were related to treatment. Increased liver weight in F given the LD was also noted as a treatment-related effect.	Terrill et al. (1991)

Abbreviations: F = female(s); HD = high dose; LD = low dose; M = male(s); MD = mid-dose; n.p. = not provided

9.2 Reproductive and Teratological Effects

The details of these studies are presented in **Table 6**.

In a 2-year study evaluating the reproductive effects of 1,3-dichloropropane in mice given intermittent oral dosing, the lowest effective dose was reported as 1.15 mmol/kg (Fisher, 2000); no further details were provided.

Doses up to 3.54 mmol 1,3-dichloropropane/kg/day for 14 days did not induce effects on the male rat reproductive system (Shell Oil Co., 1979).

9.3 Carcinogenicity

No carcinogenicity studies of 1,1-dichloropropene, 1,3-dichloropropane, or 2,2-dichloropropane were located.

9.4 Genotoxicity

The details of these studies are presented in **Table 7**.

9.4.1 Prokaryotic Systems

1,1-dichloropropene was mutagenic in *Salmonella typhimurium* at a concentration of 750 nL/plate; information on strain and metabolic status was not provided (Lewis, 2000).

1,3-Dichloropropane was mutagenic in *S. typhimurium* strain TA1535 when tested with metabolic activation at concentrations of 4.43 mol/plate and higher (Dean et al., 1985; Shell Oil Co., 1986). However, no mutagenicity was detected in strain TA1535 without metabolic activation or in strains TA98, TA 100, TA1537, TA1538 with or without metabolic activation when tested at concentrations up to 35.4 mol/plate (Buijs et al., 1984; Dean et al., 1985; Shell Oil Co., 1986). In another study, 1,3-dichloropropane was found to be mutagenic to strain TA100 at 10 mol/plate when tested without metabolic activation (Stolzenberg and Hine, 1980). Positive mutagenicity responses were also observed at doses that were cytotoxic (i.e., 10 mol/plate with metabolic activation and 100 mol/plate with or without metabolic activation).

Table 6. Reproductive Toxicity and Teratogenicity of 1,3-Dichloropropane

Species (Strain and Age)	Number and Sex of Animals	Chemical Form and Purity	Route, Dose, and Duration	Observation Period	Results/Comments	Reference
Mice (strain and age n.p.)	n.p.	1,3-dichloropropane, purity n.p.	Oral dose (amount n.p.) administered intermittently for 2 yr.	n.p.	Lowest effective dose was 130 g/kg (1.15 mmol/kg). Additional details n.p.	Fisher (2000)
Rats (Wistar, age n.p.)	10 M per treatment group	1,3-dichloropropane, purity n.p.	0, 100, or 400 mg/kg/day by gavage for 14 days	Observed on Day 15	No effects were observed w/ regard to testis weights, morphology, or detailed macroscopic and microscopic evaluation of the kidneys, testes, epididymis, ductuli efferentes, or vas deferens.	Shell Oil Co. (1979)

Abbreviations: M = male(s); n.p. = not provided; w/ = with; yr = year(s)

Table 7. Genotoxicity Studies of 1,1-Dichloropropene, 1,3-Dichloropropane, and 2,2-Dichloropropane

Test System or Species, Strain, and Age	Biological Endpoint	S9 Metabolic Activation	Chemical Form and Purity	Dose	Endpoint Response	Comments	Reference
9.4.1 Prokaryotic Systems							
Salmonella typhimurium, strain n.p.	*his* gene mutations	n.p.	1,1-dichloropropene, purity n.p.	750 nL/plate	Positive	**From:** Biochem. Pharmacol. 35:195, 1986.	Lewis (2000)
S. typhimurium strains TA1530 and TA1535	*his* gene mutations	-	1,3-dichloropropane, purity n.p.	10 mol/plate	Negative	Spot test	Buijs et al. (1984)
S. typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538	*his* gene mutations	+/-	1,3-dichloropropane, 99% pure	Up to 4000 g/plate (35.4 mol/plate)	Positive in strain TA1535 w/ MAS Negative in TA1535 w/o MAS Negative in all other strains w/ or w/o MAS	Positive response was induced in a dose-dependent manner at concentrations of 500 g/plate (4.43 mol/plate) and higher.	Dean et al. (1985); Shell Oil Co. (1986)
S. typhimurium strain TA100	*his* gene mutations	+/-	1,3-dichloropropane, 99% pure	1, 10, or 100 mol/plate	Positive (w/ and w/o MAS)	The 10 and 100 mol/plate concentrations were cytotoxic when testing w/ MAS. The 100 mol/plate dose completely inhibited bacterial growth when testing w/o MAS. The only positive response at a level that was not cytotoxic was 10 mol/plate w/o MAS. It should be noted that statistics were not used to evaluate the significance of the observed responses.	Stolzenberg and Hine (1980)
S. typhimurium, strain n.p.	*his* gene mutations	n.p.	1,3-dichloropropane, purity n.p.	100 g/plate (0.885 mol/plate)	Positive		Fisher (2000)
Escherichia coli strains WP2 and WP2 uvrA	Mutations (type unspecified)	+/-	1,3-dichloropropane, purity n.p.	Up to 4000 g/plate (35.4 mol/plate)	Negative		Shell Oil Co. (1986)

Table 7. Genotoxicity Studies of 1,1-Dichloropropene, 1,3-Dichloropropane, and 2,2-Dichloropropane (Continued)

Test System or Species, Strain, and Age	Biological Endpoint	S9 Metabolic Activation	Chemical Form and Purity	Dose	Endpoint Response	Comments	Reference
E. coli strain PQ37	Induction of *lexA*-controlled SOS repair	n.p.	1,3-dichloropropane, purity n.p.	n.p.	Negative		von der Hude et al. (1988)
Bacillus subtilis strain H17 (rec+) and M45 (rec-)	DNA damage	+/-	1,3-dichloropropane, purity n.p.	n.p.	Positive (w/ MAS) Negative (w/o MAS)	R_{50}=1.25 (w/o MAS) and 1.94 (w/ MAS) Typical R_{50}s for strong and non-DNA damaging substances are 7.01 (i.e., mitomycin C) and 1.01 (i.e., kanamycin), respectively (both w/o MAS).	Matsui et al. (1989)
9.4.2 Lower Eukaryotic Systems							
Aspergillis nidulans strain P1	Aneuploidy assessed by mitotic chromosome malsegregation	-	1,1-dichloropropene, 97% pure	n.p.	Negative	Cytotoxicity, measured as D_{37}, was induced at 6.6 mM. Lowest effective concentration inducing mitotic arrest was 5.0 mM.	Crebelli et al. (1995)
A. nidulans, strain n.p.	Aneuploidy assessed by mitotic chromosome malsegregation	-	1,1-dichloropropene, purity n.p.	n.p.	Negative	Cytotoxicity and mitotic arrest were reported.	Rosenkranz and Klopman (1996)
A. nidulans strain P1	Aneuploidy assessed by mitotic chromosome malsegregation	-	1,3-dichloropropane, 99% pure	n.p.	Negative	Cytotoxicity, measured as D_{37}, was induced at 10.5 mM. Lowest effective concentration inducing mitotic arrest was 13.7 mM.	Crebelli et al. (1995)
A. nidulans, strain n.p.	Aneuploidy assessed by mitotic chromosome malsegregation	-	1,3-dichloropropane, purity n.p.	n.p.	Negative	Cytotoxicity and mitotic arrest were not induced.	Rosenkranz and Klopman (1996)

Table 7. Genotoxicity Studies of 1,1-Dichloropropene, 1,3-Dichloropropane, and 2,2-Dichloropropane (Continued)

Test System or Species, Strain, and Age	Biological Endpoint	S9 Metabolic Activation	Chemical Form and Purity	Dose	Endpoint Response	Comments	Reference
Saccharomyces cerevisiae strain JD1	Chromosomal effects (type not specified)	+/-	1,3-dichloropropane, 99% pure	Up to 5.0 mg/mL (44.3 mM)	Negative		Dean et al. (1985); Shell Oil Co (1986)
Drosophila melanogaster strains Berlin K and Berlin K x Basc	Sex-linked recessive lethal mutations	NA	1,3 dichloropropane, purity n.p.	800 or 2400 mg/m^3 (173 or 519 ppm) for 6 h or 820 or 990 mg/m^3 (177 or 214 ppm) for 96 h by inhalation	Negative		Kramers et al. (1991)
A. nidulans strain P1	Aneuploidy assessed by mitotic chromosome malsegregation	-	2,2-dichloropropane, 98% pure	n.p.	Negative	Cytotoxicity, measured as D_{37}, was induced at 19.2 mM. Lowest effective concentration inducing mitotic arrest was 17.2 mM.	Crebelli et al. (1995)
A. nidulans, strain n.p.	Aneuploidy assessed by mitotic chromosome malsegregation	-	2,2-dichloropropane, purity n.p.	n.p.	Negative	Cytotoxicity and mitotic arrest were not induced.	Rosenkranz and Klopman (1996)
9.4.3 Mammalian Systems In Vitro							
Mouse lymphoma cells	Mutations	+	1,3-dichloropropane, purity n.p.	11,600 g/L (0.103 mM)	Positive		Fisher (2000)
Rat liver RL4 cells	Chromosome aberrations	-	1,3-dichloropropane, 99% pure	0, 125, 250, or 500 g/mL (1, 1.12, 2.21, or 4.43 mM)	Negative		Dean et al., 1985); Shell Oil Co (1986)
Chinese hamster V79 cells	SCE induction	+/-	1,3-dichloropropane, 98% pure	3.3, 6.6, 10.0 mM	Positive (w/ and w/o MAS)	A 16.6 mM dose was also considered. However, it was insoluble and was therefore not tested.	von der Hude et al. (1987)

Table 7. Genotoxicity Studies of 1,1-Dichloropropene, 1,3-Dichloropropane, and 2,2-Dichloropropane (Continued)

Test System or Species, Strain, and Age	Biological Endpoint	S9 Metabolic Activation	Chemical Form and Purity	Dose	Endpoint Response	Comments	Reference
Chinese hamster V79 cells	SCE induction	n.p.	1,3-dichloropropane, purity n.p.	3300 mol/L	Positive		Fisher (2000)
CHO cells	SCE induction	n.p.	1,3-dichloropropane, purity n.p.	113 mg/L (1 mM)	Positive	660 mg/L (5.84 mM) was cytotoxic.	Fisher (2000)
Human lymphocytes	Induction of DNA single-strand breaks and alkali-labile sites	+/-	1,3-dichloropropane, 99% pure	n.p.	Positive (w/ and w/o MAS)	The alkaline Comet assay (pH>13) was used. The lowest effective concentration, both w/ and w/o MAS, was 0.5 mM. Note: The authors did not specify the unit of the concentration reported. It is assumed that the unit was mM since all other compounds were reported in mM quantities.	Tafazoli et al. (1998)
Human lymphocytes	Micronuclei induction	+/-	1,3-dichloropropane, 99% pure	0, 0.5, 2, or 4 mM (w/o S9) 0, 0.5, 1, 2, 4, or 6 mM (w/ S9)	Positive (w/ and w/o MAS)	The 4 and 6 mM doses were considered to be cytotoxic in the experiments w/ MAS because they induced greater than a 50% decline in the cell division rate. Although statistically significant increases in micronuclei induction were observed w/ and w/o MAS, the response was not dose-dependent.	Tafazoli and Kirsch-Volders (1996)

Table 7. Genotoxicity Studies of 1,1-Dichloropropene, 1,3-Dichloropropane, and 2,2-Dichloropropane (Continued)

Test System or Species, Strain, and Age	Biological Endpoint	S9 Metabolic Activation	Chemical Form and Purity	Dose	Endpoint Response	Comments	Reference
Human lymphocytes	Induction of DNA single-strand breaks and alkali-labile sites	+/-	1,3-dichloropropane, 99% pure	0, 0.5, or 2 mM	Positive (w/ and w/o MAS)	The alkaline Comet assay (pH>13) was used. Although statistically significant increases in DNA damage were observed w/ and w/o MAS, a significant dose-response was only observed w/ MAS.	Tafazoli and Kirsch-Volders (1996)
Human lymphoblastoid cell lines AHH-1, H2E1, and MCL-5	Micronuclei induction	The cell lines are metabolically competent.	1,3-dichloropropane, purity n.p.	Up to 10.00 mM	Positive (AHH-1 and H2E1 cell lines) Negative (MCL-5 cell line)	Kinetochore staining and *in situ* hybridization indicated that the micronuclei produced were primarily kinetochore- and centromere-negative. The authors felt that this may indicate a direct-acting genotoxic effect, without requiring metabolic activation. The authors also felt that the negative result in the MCL-5 cell line was probably due to the production of a metabolite that was less genotoxic than 1,3-dichloropropane.	Doherty et al. (1996)
9.4.4 Mammalian Systems In Vivo							
Mice (strain Crl: CD-1 [ICR] BR, age n.p.)	Micronucleated PCEs	NA	1,3-dichloropropane, 99% pure	320 to 560 mg/kg (2.83 or 4.96 mmol/kg) i.p.	Negative	Animals were sacrificed 24 or 48 after treatment, bone marrow was extracted from femurs, and PCEs were isolated and scored.	Crebelli et al. (1999)

Abbreviations: CHO = Chinese hamster ovary; D_{37} = dose inducing one lethal hit per cell (37% of survivors); MAS = metabolic activation system; NA = not applicable; n.p. = not provided; PCEs = polychromatic erythrocytes; SCE = sister chromatid exchange; R_{50} = ratio of the 50% survival concentration for the rec^+ (H17) strain divided by the 50% survival concentration for the rec^- (M45) strain; w/ = with; w/o = without

1,3-Dichloropropane was not mutagenic when tested in two *Escherichia coli* experiments (Fisher, 2000; Shell Oil Co., 1986). It was found to induce DNA damage, however, in *Bacillus subtilis* when tested with, but not without, metabolic activation (Matsui et al., 1989).

9.4.2 Lower Eukaryotic Systems

1,3-Dichloropropane was negative in studies testing for:

aneuploidy in *Aspergillus nidulans* without metabolic activation (Crebelli et al., 1995; Rosenkranz and Klopman, 1996);

chromosomal effects in *Saccharomyces cerevisiae* with or without metabolic activation (Dean et al., 1985; Shell Oil Co., 1986); or

sex-linked recessive lethal mutations in *Drosophila melanogaster* (Kramers et al., 1991).

1,1-Dichloropropene and 2,2-Dichloropropane also did not induce aneuploidy in *A. nigulans* (Crebelli et al., 1995; Rosenkranz and Klopman, 1996).

9.4.3 Mammalian Systems *In Vitro*

1,3-Dichloropropane was found to induce:

mutations in mouse lymphoma cells with metabolic activation (Fisher, 2000);

sister chromatid exchanges in Chinese hamster V79 cells with and without metabolic activation (von der Hude et al., 1987; Fisher, 2000) and in Chinese hamster ovary cells where metabolic status was not provided (Fisher, 2000);

DNA single-strand breaks and alkali-labile sites in human lymphocytes with and without metabolic activation (Tafazoli et al., 1998; Tafazoli and Kirsch-Volders, 1996); and

micronuclei in human lymphocytes with and without metabolic activation (Tafazoli and Kirsch-Volders, 1996; Doherty et al., 1996). Doherty et al. (1996) hypothesized that *in vitro* production of micronuclei may indicate the ability of these metabolically competent cell lines to express cytochrome P450 and metabolize halogenated hydrocarbones to genotoxic compounds, including clastogens and aneugens.

1,3-Dichloropropane did not induce chromosomal aberrations in rat liver RL4 cells (Dean et al., 1985; Shell Oil Co., 1986).

9.4.4 Mammalian Systems *In Vivo*

A single 2.83 or 4.96 mmol 1,3-dichloropropane/kg i.p. did not induce micronucleated polychromatic erythrocytes in mice (Crebelli et al., 1999).

9.5 Immunotoxicity

No immunotoxicity studies of 1,1-dichloropropene, 1,3-dichloropropane, or 2,2-dichloropropane were located.

9.6 Other Data

9.6.1 Membrane Effects

1,3-Dichloropropane (0.001 to 10 M) did not induce lipid peroxidation in cultured rat microsomes (Crebelli et al., 1995).

9.6.2 Cytotoxicity

The lowest cytotoxic concentration of 1,3-dichloropropane was presumably 0.5 mM, when tested on cultured human lymphocytes with and without metabolic activation (Tafazoli et al., 1998). Since the authors did not specify the unit of the concentration reported, it was assumed that the unit was mM because other compounds tested were reported in mM concentrations.

10.0 STRUCTURE-ACTIVITY RELATIONSHIPS

In a study evaluating the toxicity of 13 chlorinated alkanes using fish, daphnia, algae, and photobacteria, Freitag et al. (1994) concluded that the level of toxicity increases with higher numbers of chlorine atoms in the molecule, as well as higher numbers of chlorine atoms concentrated at one carbon atom. 1,3-Dichloropropane ranked eighth in terms of overall toxicity.

Buijs et al. (1984) evaluated the mutagenic potential of 18 dihaloalkanes using spot-tests in *S. typhimurium* strains TA1530, TA1535, and TA100. A strong correlation was found between mutagenic behavior and carbon chain length as well as the halogen involved. 1,3-Dichloropropane was not found to be mutagenic. Brominated and iodinated hydrocarbons were found to be more mutagenically active. In a similar study, all 2- or 3-carbon halocarbon compounds that contained bromine were more mutagenically active in *S. typhimurium* TA100 than those that contained chlorine (Stolzenberg and Hine, 1980). Those that contained fluorine exhibited even less mutagenic ability.

While Rosenkranz and Klopman (1996) concluded that there were commonalities in the structural determinants associated with cytotoxicity and mitotic arrest in *Aspergillis nidulans*, there were no such similarities between these and genotoxicity, as measured by induction of aneuploidy. Thirty-five chlorinated alkanes and alkenes were investigated; 1,3-dichloropropane and 2,2-dichloropropane tested negative for the three measured endpoints, while 1,1-dichloropropene tested positive for mitotic arrest, but negative for aneuploidy and cytotoxicity.

In a study of the lipid peroxidation-inducing potential of 27 halogenated hydrocarbons, electronic and structural parameters related to the ease of homolytic cleavage of the carbon-halogen bond played a pivotal role in the ability of the halogenated hydrocarbons to induce lipid peroxidation *in vitro* (Crebelli et al., 1995). 1,3-Dichloropropane was found to have no effect at the doses tested. Those chemicals that were most potent, in decreasing order, include chlorodibromofluoromethane, bromodichloromethane, chlorodibromomethane, and carbon tetrachloride.

Using a database that reported the mutagenic activity of 209 chemicals in mouse lymphoma cells, Henry et al. (1998) reported that 1,3-dichloropropane was inactive and did not contain any of the 13 biophores associated with mutagenic effects. The biophores were specific chemical structures usually involving either double bonding along the carbon chain or ring, or close proximity of chlorine atoms to each other within the molecule.

1,3-Dichloropropene (technical grade with 1.0% epicholohydrin) is reasonably anticipated to be a human carcinogen (NTP, 2000; NTP 269, 1985) as is 1,2,3-trichloropropane (NTP, 2000; NTP384, 1993). In two-year carcinogenicity studies, there was no evidence for the carcinogenicity of 1,2-dichloropropane (62 and 125 mg/kg body weight) in F344/N rats and equivocal evidence of carcinogenicity in female rats dosed with 250 mg/kg 1,2-dichloropropane (NTP, 2000; NTP 263, 1986). Increased incidences of hepatocellular neoplasms, primarily adenomas, indicated some evidence of carcinogenicity in male and female B6C3F_1 mice (NTP, 2000; NTP 263, 1986).

11.0 ONLINE DATABASES AND SECONDARY REFERENCES

11.1 Online Databases

Chemical Information System Files

SANSS (Structure and Nomenclature Search System)
TSCATS (Toxic Substances Control Act Test Submissions)

DIALOG Files

CEH (Chemical Economics Handbook)

National Library of Medicine Databases

EMIC and EMICBACK (Environmental Mutagen Information Center)

STN International Files

BIOSIS	LIFESCI
CABA	MEDLINE
CANCERLIT	NIOSHTIC
CAPLUS	PROMT
CHEMLIST	Registry
EMBASE	RTECS
HSDB	TOXLINE

TOXLINE includes the following subfiles:

Toxicity Bibliography	TOXBIB
International Labor Office	CIS
Hazardous Materials Technical Center	HMTC
Environmental Mutagen Information Center File	EMIC
Environmental Teratology Information Center File (continued after 1989 by DART)	ETIC
Toxicology Document and Data Depository	NTIS
Toxicological Research Projects	CRISP
NIOSHTIC®	NIOSH
Pesticides Abstracts	PESTAB
Poisonous Plants Bibliography	PPBIB
Aneuploidy	ANEUPL
Epidemiology Information System	EPIDEM
Toxic Substances Control Act Test Submissions	TSCATS
Toxicological Aspects of Environmental Health	BIOSIS
International Pharmaceutical Abstracts	IPA
Federal Research in Progress	FEDRIP
Developmental and Reproductive Toxicology	DART

In-House Databases

CPI Electronic Publishing Federal Databases on CD
Current Contents on Diskette¤
The Merck Index, 1996, on CD-ROM

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APPENDIX A: UNITS AND ABBREVIATIONS

°C = degrees Celsius
µg/L = microgram(s) per liter
µg/m^3 = microgram(s) per cubic meter
µg/mL = microgram(s) per milliliter
µM = micromolar
bw = body weight
DOT = U.S. Department of Transportation
EPA = U.S. Environmental Protection Agency
F = female(s)
g = gram(s)
g/mL = gram(s) per milliliter
h = hour(s)
i.p. = intraperitoneal(ly)
i.v. = intravenous(ly)
kg = kilogram(s)
L = liter(s)
LC_{50} = lethal concentration for 50% of test animals
LD_{50} = lethal dose for 50% of test animals
lb = pound(s)
M = male(s)

mg/kg = milligram(s) per kilogram
mg/m^3 = milligram(s) per cubic meter
mg/mL = milligram(s) per milliliter
mL/kg = milliliter(s) per kilogram
mm = millimeter(s)
mM = millimolar
mmol = millimole(s)
mmol/kg = millimoles per kilogram
mo = month(s)
mol = mole(s)
mol. wt. = molecular weight
NA = not applicable
NIEHS = National Institute of Environmental Health Sciences
nm = nanometer(s)
n.p. = not provided
ppb = parts per billion
ppm = parts per million
QSARs = quantitative structure-activity relationships
s = second(s)
s.c. = subcutaneous(ly)
wk = week(s)
yr = year(s)