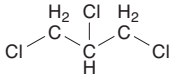
1,2,3-Trichloropropane

CAS No. 96-18-4

Reasonably anticipated to be a human carcinogen

First listed in the *Eighth Report on Carcinogens* (1998)



Carcinogenicity

1,2,3-Trichloropropane is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Oral exposure to 1,2,3-trichloropropane caused tumors at several different tissue sites in mice and rats. Administration of 1,2,3-trichloropropane by stomach tube increased the combined incidence of benign and malignant tumors of the forestomach (squamous-cell papilloma and carcinoma) in mice and rats of both sexes. In mice of both sexes, it also increased the combined incidence of benign and malignant liver tumors (hepatocellular carcinoma and adenoma) and caused benign Harderian-gland tumors (adenoma). In rats of both sexes and in female mice, it caused benign and/or malignant tumors of the oral mucosa (squamous-cell papilloma and/or carcinoma). In rats, oral exposure to 1,2,3-trichloropropane also caused cancer of the Zymbal gland (carcinoma) in both sexes, cancer of the mammary gland (carcinoma) in females, and benign tumors (adenoma) of the kidney and pancreas in males, and it increased the combined incidence of benign and malignant tumors (adenoma and carcinoma) of the preputial gland in males and the clitoral gland in females. In female mice, it also caused benign and malignant tumors of the uterus (adenoma, stromal polyp, and adenocarcinoma) (NTP 1993, IARC 1995, Irwin *et al.* 1995).

Since 1,2,3-trichloropropane was listed in the *Eighth Report on Carcinogens,* an additional study in experimental animals has been identified. Exposure to 1,2,3-trichloropropane in the aquarium water of guppies *(Poecilia reticulata)* and medaka *(Oryzias latipes)* caused liver tumors in males and females of both species and benign gallbladder tumors (papillary adenoma) in medaka of both sexes (NTP 2005).

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to 1,2,3-trichloropropane.

Studies on Mechanisms of Carcinogenesis

1,2,3-Trichloropropane caused gene mutations in bacteria, yeast, and mammalian cells and sister chromatid exchange, chromosomal aberrations, micronucleus formation, and morphological transformation in mammalian cells *in vitro* (IARC 1995, Doherty *et al.* 1996). 1,2,3-Trichloropropane was active almost exclusively in the presence of mammalian microsomal metabolic activation or when tested in metabolically competent cells. In rats and mice exposed by gavage or intraperitoneal injection, 1,2,3-trichloropropane caused DNA damage, including formation of DNA adducts, in several different tissues (IARC 1995, La *et al.* 1995). 1,2,3-Trichloropropane also caused cell proliferation at several tissue sites in rats and mice exposed by gavage and rats exposed by inhalation (Johannsen *et al.* 1988, NTP 1993, Irwin *et al.* 1995). 1,2,3-Trichloropropane was reported not to cause dominant lethal mutations in male rats (IARC 1995).

Several metabolites of 1,2,3-trichloropropane, including 1,3-dichloroacetone, caused genetic damage in various short-term test systems (IARC 1995). 1,3-Dichloroacetone is produced by human liver microsomes, although at a lower rate of formation than in rats (Weber and Sipes 1992). Two 1,2,3-trichloropropane analogues, 1,2-dibromo-3-chloropropane and 1,2-dibromoethane (ethylene dibromide), are listed in the Report on Carcinogens as *reasonably anticipated to be a human carcinogen.*

Properties

1,2,3-Trichloropropane is a halogenated alkane that exists at room temperature as a colorless to straw-colored liquid with an odor similar to that of trichloroethylene or chloroform (IPCS 2003). It is slightly soluble in water and soluble in chloroform, ethanol, and diethyl ether (IARC 1995). It is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of 1,2,3-trichloropropane are listed in the following table.

Property	Information
Molecular weight	147.4
Specific gravity	1.3889 at 20°C/4°C
Melting point	–14.7°C
Boiling point	156.85°C
Log K_{ow}	2.27
Water solubility	1.8 g/L at 25°C
Vapor pressure	3.69 at 25°C
Vapor density relative to air	5.1

Source: HSDB 2009.

Use

1,2,3-Trichloropropane is used primarily as a chemical intermediate in the production of polysulfone liquid polymers, dichloropropene, and hexafluoropropylene, and as a cross-linking agent in the synthesis of polysulfides (ATSDR 1992). No data were found to indicate the extent to which 1,2,3-trichloropropane is currently used for these purposes. In the past, 1,2,3-trichloropropane was used primarily as a solvent and extracting agent (ATSDR 1992, IARC 1995). As a solvent, it was commonly used as a cleaning and maintenance solvent, paint and varnish remover, and degreasing agent. No indication was found that it continues to be used for these purposes (ATSDR 1992). 1,2,3-Trichloropropane was formulated with dichloropropenes in the manufacture of the soil fumigant D-D (IARC 1995), which is no longer available in the United States (Sine 1991).

Production

Estimates for the production of 1,2,3-trichloropropane in the United States in 1977 ranged from 21 million to 110 million pounds (ATSDR 1992). In 2009, 1,2,3-trichloropropane was produced by five manufacturers worldwide, including two in the United States (SRI 2009), and was available from 22 suppliers, including 15 U.S. suppliers (ChemSources 2009). Reports filed under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of 1,2,3-trichloropropane totaled 10 million to 50 million pounds in 1986, 1990, and 1998 and 1 million to 10 million pounds in 2002 (EPA 2004). No data were found on U.S. imports or exports of 1,2,3-trichloropropane.

1,2,3-Trichloropropane may also be produced in significant quantities as a by-product of the production of other compounds, such as epichlorohydrin, dichloropropene, propylene oxide, propylene chlorohydrin, dichlorohydrin, and glycerol (ATSDR 1992, IPCS 2003).

Exposure

The general population may potentially be exposed to low levels of 1,2,3-trichloropropane through ingestion of contaminated well water or inhalation of contaminated air. Exposure is more likely for individuals who live near facilities that use or produce 1,2,3-trichloropropane or near hazardous waste disposal facilities (ATSDR 1992). In the U.S. Food and Drug Administration's Total Diet Study, 1,2,3-trichloropropane was detected in one sample of boiled fresh or frozen green beans at a concentration of 0.018 ppm (18 µg/kg) (FDA 2006). In the past, inhalation and dermal exposure likely occurred during the use of consumer products that contained 1,2,3-trichloropropane, such as certain paint and varnish removers and cleaning agents; however, it has been reported that 1,2,3-trichloropropane is no longer used in consumer products (ATSDR 1992).

Releases to the environment are likely to occur as a result of manufacture, formulation, and use of products containing 1,2,3-trichloropropane as a contaminant, such as soil fumigants and well-drilling aids (HSDB 2009, IPCS 2003). According to EPA's Toxics Release Inventory, environmental releases of 1,2,3-trichloropropane from 1995 to 2003 ranged from a low of 2,091 lb in 1996 to a high of 98,000 lb in 2002 (TRI 2009). The largest releases have been to air. In 2003, seven facilities reported releases of 14,256 lb, of which 65% was released to air and 26% to surface water; 98% of waste containing 1,2,3-trichloropropane was managed on site. If released to air, 1,2,3-trichloropropane is expected to exist as a vapor, because of its high vapor pressure (HSDB 2009). In air, it may react with photochemically produced hydroxyl radicals, with an estimated half-life of 46 days. If released to water, it will most likely volatilize, with an estimated half-life of 6.7 hours in river models and 5.7 days in lake models. If released to land, it is expected either to volatilize from surface soil or to leach into groundwater.

No measurements of 1,2,3-trichloropropane in air in the United States were found. In 1976, 1,2,3-trichloropropane was detected qualitatively in 1 of 30 surface-water samples from the Delaware, Schuylkill, and Lehigh rivers (ATSDR 1992). It was found in nearly half of municipal sewage sludge samples collected in Michigan in 1980, at a median concentration of 0.35 mg/kg on a dry-weight basis, and in U.S. groundwater wells at concentrations of up to 10 µg/L (ATSDR 1992, Tesoriero *et al.* 2001). In Osaka, Japan, it was found in 18 samples of surface water from urban rivers and their estuaries, at concentrations ranging from the detection limit (0.18 µg/L) to 100 µg/L (Yamamoto *et al.* 1997). 1,2,3-Trichloropropane has been identified as a contaminant at eight hazardous-waste sites on EPA's National Priorities List (ATSDR 1992).

1,2,3-Trichloropropane is manufactured in closed systems; therefore, occupational exposures are more likely to occur at facilities where it is used than at facilities where it is produced (ATSDR 1992). Direct handling of 1,2,3-trichloropropane or products containing 1,2,3-trichloropropane may occur during purification, formulation of products, sampling, quality control, packaging and storage, leakage of equipment, startup and shutdown procedures, maintenance, cleanup, and spills or other facility emergencies. The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 492 workers (in the Chemicals and Allied Products industry), including 10 women, potentially were exposed to 1,2,3-trichloropropane (NIOSH 1990).

Regulations

Coast Guard, Department of Homeland Security

Minimum requirements have been established for safe transport of 1,2,3-trichloropropane on ships and barges.

Environmental Protection Agency (EPA)

Clean Air Act

New Source Performance Standards: Manufacture or use is subject to certain provisions for the control of volatile organic compound emissions.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.

Resource Conservation and Recovery Act

Listed as a hazardous constituent of waste.

Occupational Safety and Health Administration (OSHA)

While this section accurately identifies OSHA's legally enforceable PELs for this substance in 2010, specific PELs may not reflect the more current studies and may not adequately protect workers.
Permissible exposure limit (PEL) = 50 ppm (300 mg/m^3).

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 0.005 ppm.

National Institute for Occupational Safety and Health (NIOSH)

Recommended exposure limit (REL) = 10 ppm (60 mg/m^3).
Immediately dangerous to life and health (IDLH) limit = 100 ppm.
Potential for dermal absorption.
Listed as a potential occupational carcinogen.

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