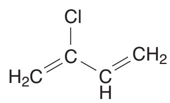
Chloroprene

CAS No. 126-99-8

Reasonably anticipated to be a human carcinogen

First listed in the *Ninth Report on Carcinogens* (2000)

Also known as 2-chloro-1,3-butadiene



Carcinogenicity

Chloroprene is *reasonably anticipated to be a human carcinogen* based on evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Inhalation exposure to chloroprene caused tumors at several different tissue sites in mice and rats. It caused lung tumors (alveolar/bronchiolar adenoma and/or carcinoma) in mice of both sexes and in male rats; kidney tumors in rats of both sexes and in male mice (renal-tubule adenoma); and mammary-gland tumors in female rats (fibroadenoma) and mice. In rats of both sexes, it also caused tumors of the oral cavity (squamous-cell papilloma and carcinoma) and thyroid gland (follicular-cell adenoma or carcinoma). In mice, it also caused tumors of the forestomach (squamous-cell papilloma), Harderian gland (adenoma or carcinoma), and blood vessels (hemangioma and hemangiosarcoma) in both sexes and tumors of the liver (hepatocellular adenoma and carcinoma), Zymbal gland (carcinoma), skin (sarcoma), and mesentery (sarcoma) in females (NTP 1998).

Cancer Studies in Humans

Data from two early epidemiological studies suggested that occupational exposure to chloroprene may increase the risks of cancer of the liver, lung, and digestive and lymphohematopoietic systems (Pell 1978, Li *et al.* 1989). Since chloroprene was listed in the *Ninth Report on Carcinogens,* additional epidemiological studies have been identified. Mortality from leukemia and liver cancer was significantly increased among shoe-manufacturing workers, and liver-cancer incidence and mortality were signficantly increased among chloroprene-production workers (Bulbulyan *et al.* 1998, 1999). However, two other cohort studies of chloroprene-production workers found no excess of liver cancer (Colonna and Laydevant 2001, Marsh *et al.* 2007a,b). These two studies reported increased risks of lung or respiratory cancer; however, the risk estimates were not statistically significant or related to exposure category in the small cohort study (Colonna and Laydevant 2001) and were significantly elevated in only one of several plants in the large multi-plant study (Marsh *et al.* (2007a,b).

Studies on Mechanisms of Carcinogenesis

Chloroprene (the 2-chloro analogue of 1,3-butadiene) caused all of the same types of tumors that 1,3-butadiene caused in mice except for lymphoma and tumors of the preputial gland and ovary (NTP 1998).

In vitro metabolism of chloroprene by mouse, rat, hamster, and human microsomes produced (1-chloroethenyl)oxirane, an epoxide that is thought to react with DNA and can be further metabolized by hydrolysis and glutathione conjugation (Himmelstein *et al.* 2001). However, many studies on the genotoxicity of chloroprene have given negative results, and positive results from earlier studies were attributed to differences in the age and purity of the chloroprene samples (Westphal 1994, NTP 1998). The mutagenicity of chloroprene in bacteria (Bartsch *et al.* 1975, 1979) was considered to be due to cyclic dimers that accumulate in aged samples (Westphal *et al.* 1994).

At the same exposure concentrations as used in the inhalation-exposure studies of cancer in mice, chloroprene did not cause sister chromatid exchange or chromosomal aberrations in mouse bone-marrow cells, nor did it increase the frequency of micronucleated erythrocytes in peripheral blood (Tice *et al.* 1988). During another inhalation-exposure study in mice and rats, chloroprene caused dominant lethal mutations in both species and chromosomal aberrations in mouse bone marrow cells (Sanotskii 1976). However, despite the largely negative findings for genotoxicity, chloroprene-induced lung and Harderian-gland tumors from mice had a high frequency of unique mutations of the K-*ras* proto-oncogene (NTP 1998). In addition, occupational-exposure studies reported increased frequencies of chromosomal aberrations in the lymphocytes of workers (IARC 1979).

Properties

Chloroprene is a halogenated alkene that exists at room temperature as a clear colorless liquid with a pungent ether-like odor. It is practically insoluble in water, soluble in alcohol, and miscible with acetone, benzene, and ethyl ether. It is highly flammable and polymerizes on standing, making it unstable in the environment (Akron 2009). Physical and chemical properties of chloroprene are listed in the following table.

Property	Information
Molecular weight	88.5[a]
Specific gravity	0.956 at 20°C/4°C[a]
Melting point	–130°C[a]
Boiling point	59°C[a]
Log K_{ow}	2.53[b]
Water solubility	0.875 g/L at 25°C[b]
Vapor pressure	215 mm Hg at 25°C[a]
Vapor density relative to air	3[a]

Sources: [a]HSDB 2009, [b]ChemIDplus 2009.

Use

The only commercial use identified for chloroprene is as a monomer in the production of the elastomer polychloroprene (neoprene), a synthetic rubber used in the production of automotive and mechanical rubber goods, adhesives, caulks, flame-resistant cushioning, construction materials, fabric coatings, fiber binding, and footwear. Other uses of this polymer include applications requiring chemical, oil, or weather resistance or high gum strength. The U.S. Food and Drug Administration permits the use of chloroprene as a component of adhesives used in food packaging and also permits the use of polychloroprene in products intended for use with food (IARC 1979, 1999, NTP 1998).

Production

In 2009, chloroprene was produced by one manufacturer each in the United States and China and two manufacturers in Europe (SRI 2009) and was available from eleven suppliers, including seven U.S. suppliers (ChemSources 2009). Reports filed between 1986 and 2002 under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of chloroprene totaled 100 million to 500 million pounds (EPA 2004).

Exposure

The routes of human exposure to chloroprene are inhalation, ingestion, and dermal contact. Chloroprene is not known to occur naturally in the environment (IARC 1999). The main sources of environmental releases are effluent and emissions from facilities that use chloroprene to produce polychloroprene elastomers. According to EPA's Toxics Release Inventory, environmental releases of chloroprene have decreased steadily from a high of over 2 million pounds in 1988 (the year reporting started). In 2007, two facilities reported chloroprene releases of over 275,000 lb, and seven facilities reported releases of 1,300 lb or less, almost all to air (TRI 2009). When released to air, chloroprene reacts with photochemically generated hydroxyl radicals, with a half-life of 18 hours, and smaller amounts are removed by reaction with ozone, with a half-life of 10 days. Based on the Henry's law constant and octanol-water partition coefficient, chloroprene is expected to be removed from water and damp soil primarily by volatilization. If released to water, chloroprene is expected to volatilize from the surface, with a half-life of 3 hours from streams and 4 days from lakes. It will not adsorb to sediment or suspended solids or bioaccumulate in aquatic organisms. If released to soil, chloroprene is expected to volatilize or may leach into groundwater (HSDB 2009). In 1991, EPA's Urban Air Toxics Monitoring Program identified chloroprene in 88 of 349 samples (25.2%), at concentrations ranging from 0.01 to 1.78 ppb (0.036 to 6.44 μg/m^3). The results were similar in 1996, but in 2000 and 2005, chloroprene was detected in only one sample.

The main source of occupational exposure to chloroprene is the manufacture of chloroprene or polychloroprene (NTP 1998). In 1977, it was estimated that 2,500 to 3,000 workers were exposed to chloroprene during its manufacture and polymerization (Infante 1977). Chloroprene monomer is manufactured in a closed system, which is then used on site to make the polymer. The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 17,700 workers, including 650 women, potentially were exposed to chloroprene or polychloroprene (NIOSH 1990). Time-weighted 8-hour average concentrations at three facilities (two in the United States and one in Northern Ireland) from 1975 to 1992 were 1 ppm in all but three samples, and chloroprene concentrations in the monomer manufacturing phase were below 1.8 ppm in all samples (Hall *et al.* 2007). During the polymer manufacturing phase, chloroprene concentrations were as high as 4.66 ppm in Northern Ireland and 3.42 ppm in the United States. By 1992, concentrations in all polymer facilities were lower (1.4 and 0.53 ppm in the United States and 0.37 ppm in Northern Ireland).

Regulations

Department of Transportation (DOT)

Chloroprene is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: Listed as a hazardous air pollutant.
New Source Performance Standards: Manufacture is subject to certain provisions for the control of volatile organic compound emissions.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 100 lb.

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) = 25 ppm (90 mg/m^3).
Potential for dermal absorption.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 10 ppm (36 mg/m^3).
Potential for dermal absorption.

National Institute for Occupational Safety and Health (NIOSH)

Ceiling recommended exposure limit = 1 ppm (3.6 mg/m^3) (15-min exposure).
Immediately dangerous to life and health (IDLH) limit = 300 ppm (1,086 mg/m^3).
Listed as a potential occupational carcinogen.

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