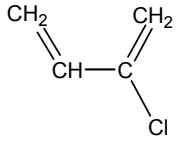
CHLOROPRENE
CAS No. 126-99-8
First Listed in the *Ninth Report on Carcinogens*



CARCINOGENICITY

Chloroprene is *reasonably anticipated to be a human carcinogen* based on evidence of benign and malignant tumor formation at multiple tissue sites in multiple species of experimental animals (NTP 1998). Inhalation exposure of rats to chloroprene vapors induced increased incidences of neoplasms of the oral cavity, thyroid gland, and kidney in males and females, neoplasms of the lung in males, and neoplasms of the mammary gland in females. Inhalation exposure of mice to chloroprene vapors induced increased incidences of neoplasms of the lung, circulatory system (hemangiomas and hemangiosarcomas), forestomach, and harderian gland in males and females, kidney neoplasms in males, and neoplasms of the mammary gland, liver, Zymbal gland, skin, and mesentery in females.

There is limited evidence for the carcinogenicity of chloroprene in humans. Data from two studies suggest that occupational exposure to chloroprene may increase cancer risk for digestive and lymphatic/hematopoietic tumors (Pell 1978) and for liver, lung, and lymphatic tumors (Li *et al*. 1989). However, the risk of cancer associated with occupational exposure to chloroprene was evaluated in one U.S. study and one Russian study; this research failed to indicate a consistent excess of cancer at any site (IARC 1999).

ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

Recent studies on the genotoxicity of chloroprene have been uniformly negative; conflicting results with earlier studies have been attributed to differences in the age and purity of the test samples. Positive mutagenicity results of chloroprene in bacteria (Bartsch *et al*. 1975, 1979) were considered to be due to cyclic dimers that accumulate in aged samples (Westphal *et al*. 1994). At the exposure concentrations used in the cancer inhalation studies, chloroprene did not induce sister chromatid exchanges or chromosomal aberrations in mouse bone marrow cells, nor did it increase the frequency of micronucleated erythrocytes in peripheral blood (Tice *et al*. 1988). Oxidation of chloroprene to epoxide intermediates has been postulated to occur based on the detection of alkylated derivatives of the trapping agent 4-(4-nitrobenzyl)pyridine in incubations of chloroprene and mouse liver microsomes (Bartsch *et al*. 1979). Chloroprene-induced lung and harderian gland neoplasms in mice had a high frequency of unique K-*ras* mutations (NTP 1998). Chloroprene (chemical name: 2-chloro-1,3-butadiene) induced all of the types of tumors that were induced by 1,3-butadiene in mice except for lymphomas and ovarian neoplasms.

No data were available that would suggest that the mechanisms thought to account for tumor induction by chloroprene in experimental animals would not also operate in humans.

PROPERTIES

Chloroprene is a colorless liquid with a pungent, ethereal odor. It is slightly soluble in water and miscible in ethanol and diethyl ether (Lewis 1992, HSDB, 2000). Chloroprene has a melting point of -130°C and a boiling point of 59.4°C (Johnson 1979a, Lewis 1992). It is a highly dangerous fire hazard. When exposed to heat or flame, it is explosive in vapor form (Lynch 1997 personal communication). Chloroprene will rapidly auto-oxidize in air to form acidic materials and unstable peroxides, which catalyze exothermic polymerization of the monomer. It will also polymerize at room temperature to produce cyclic dimers or open-chain, high molecular weight products. When heated to decomposition, chloroprene emits hydrogen chloride (HSDB 2000).

USE

Chloroprene is primarily used 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 goods, fabric coatings, sealants for dams or locks in waterways, roof coatings, fiber binding, and footwear. Other uses include applications requiring chemical, oil, weather resistance, or high gum strength (IARC 1979, 1999, Johnson 1979a, b, Budavari 1996, NTP 1998).

PRODUCTION

In 1995 there was one commercial producer of chloroprene in the United States (SRI 1996). Other plants produced chloroprene for on-site use and processing, as a by-product of vinyl chloride production, or as a manufacturing impurity (TRI95 1997). Used almost exclusively to produce polychloroprene, chloroprene is sold to only three U.S. companies for polychloroprene manufacture; less than 20 lb/yr is sold for research applications. The total estimated production of polychloroprene from 1986 to 1988 was approximately 250 to 300 million lb (113,000 to 136,000 Mg [metric tons]), and the volume from 1995 to 1996 was approximately 200 to 250 million lb (90,700 to 113,000 Mg) (Lynch 1997 personal communication). These production numbers are higher than those given for U.S. polychloroprene shipments, which represent only off-site transfers, based on information from the International Institute of Synthetic Rubber Producers (e.g., 10,000 Mg from 1995 to 1996) (Chem. Eng. News 1997). Chem Sources (2001) listed eight U.S. suppliers for chloroprene.

EXPOSURE

Chloroprene is not known to occur naturally in the environment (HSDB 2000). The primary route of potential human exposure to chloroprene is inhalation. The effluent and emissions from facilities that use chloroprene to produce polychloroprene elastomers are the main sources of environmental releases of chloroprene. Of 14 facilities reporting atmospheric releases of chloroprene in 1995, eight plants reported individual atmospheric releases from 2 to 481,871 lb (0.0009 to 218.6 Mg), for a total release of 983,888 lb (446.3 Mg). Three plants in Kentucky, Texas, and Louisiana, each reporting atmospheric releases of >100,000 lb, accounted for most of the reported chloroprene releases. One of the sites is a producer and the other two sites convert chloroprene to polychloroprene. One of the 14 facilities also reported a chloroprene release consisting of 60,000 lb (27.2 Mg) by injection in deep wells, while another facility released 5,104 lb (2.315 Mg) to land (TRI95 1997). In 1999, nine of 11 reporting facilities

reported a total release of 907,146 lb (411.5 Mg) of chloroprene to the atmosphere. Two plants, both reporting under the synthetic rubber manufacturing code (SIC 2822), accounted for 99.9% of the total air emissions. One facility reported underground injections of 29,000 lb (13.2 Mg) and no reports of releases to land were made (TRI99 2001).

Volatilization is the primary mechanism of removal of chloroprene from water. Chemical hydrolysis, adsorption to suspended solids or sediments, or bioaccumulation in aquatic animals is not expected to occur. If released to soil, chloroprene should be susceptible to removal by rapid volatilization and transport by leaching into groundwater. In the atmosphere, the primary mechanism of chloroprene removal is reaction with photochemically generated hydroxyl radicals with smaller amounts removed by reaction with ozone. Formaldehyde, 1-chloroacrolein, glyoxal, chloroglyoxal, and chlorohydroxy acids or aldehydes are expected products of these reactions (HSDB 2000). The Urban Air Toxics Monitoring Program (UATMP), developed in 1987 by EPA, collected 349 samples from 12 sites every 12 days for 24-hour periods from March 1990 through February 1991. Chloroprene was identified in 88 of 349 samples (25.2%). The range of concentrations was 0.01 to 1.78 ppb for samples in which chloroprene was identified with a mean of 0.26 ppb (0.94 $\mu g/m^3$). The mean concentration based on all samples was 0.06 ppb, where zero was used for samples not containing chloroprene (McAllister *et al*. 1991).

The primary potential occupational exposure to chloroprene will be that of workers manufacturing the compound or polychloroprene (NTP 1998). Infante (1977) reported that an estimated 2,500 to 3,000 workers were exposed to chloroprene during its manufacture and polymerization. The National Occupational Exposure Survey (NOES), conducted by NIOSH from 1981 to 1983, reported that an estimated 17,700 workers, including 650 females, were potentially exposed to chloroprene or polychloroprene (NIOSH 1990). Many workers were employed in auto repair services; their inclusion is probably attributable to their use of polychloroprene in belts, hoses, gaskets, and adhesives. Since residual monomer is appreciable only in polychloroprene latex (≤0.5% monomer), their inclusion may overestimate the actual number of workers exposed to chloroprene. DuPont Dow Elastomers estimated that fewer than 500 workers are exposed to chloroprene during manufacture. The company currently meets its internal control limit of 10 ppm, with the majority (>95%) of the time-weighted exposures <2 ppm (Lynch 1997 personal communication).

REGULATIONS

Chloroprene is regulated by EPA under the Clean Air Act (CAA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), and Superfund Amendments and Reauthorization Act (SARA).

The FDA allows the use of chloroprene in adhesives, assuming that there is a functional barrier between the adhesive and food or the exposure is the minimum acceptable under good manufacturing practice. Chloroprene polymers may be safely used in rubber products intended for repeated use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

NIOSH recommends a 15-minute ceiling value of 1 ppm (3.6 mg/m^3) for chloroprene. OSHA has established a permissible exposure limit (PEL) of 25 ppm (90 mg/m^3) as an 8-hour time-weighted average (TWA) for employee exposure to chloroprene. ACGIH has set the threshold limit value (TLV) at 10 ppm (36 mg/m^3). OSHA regulates the compound under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 42.

REFERENCES

Bartsch, H., C. Malaveille, R. Montesano, and L. Tomatis. Tissue-Mediated Mutagenicity of Vinylidene Chloride and 2-Chlorobutadiene in Salmonella Typhimurium. Nature Vol. 255, 1975, pp. 641-643.

Bartsch, H., C. Malaveille, A. Barbin, and G. Planche. Mutagenic and Alkylating Metabolites of Haloethylenes, Chlorobutadienes and Dichlorobutenes Produced by Rodent or Human Liver Tissues: Evidence for Oxirane Formation by P450-Linked Microsomal Mono-Oxygenases. Arch. Toxicol. Vol. 41, 1979, pp. 249-277.

Budavari, S., Ed. The Merck Index, Twelfth Edition. Merck & Co., Inc., Whitehall, NJ, 1996.

Chemical and Engineering News. Production: Mixed in 1996. Vol. 75, No. 25, 1997, pp. 40-45.

Chem Sources. Chemical Sources International, Inc. http://www.chemsources.com, 2001.

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. Chloroprene. Last updated February 8, 2000. Last review date November 7, 1991.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Some Monomers, Plastics and Synthetic Elastomers, and Acrolein. Vol. 19. 513 pp. Lyon, France: IARC, 1979.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Re-evaluation of Some Organic Chemicals, Hydrazine, and Hydrogen Peroxide. Vol. 71. 1589 pp. Lyon, France: IARC, 1999.

Infante, P.F. Mutagenic and Carcinogenic Risks Associated with Halogenated Olefins. Environ. Health Perspect. Vol. 21, 1977, pp. 251-254.

Johnson, P.R. Chlorocarbons and Chlorohydrocarbons. In: Kirk-Othmer Encyclopedia of Chemical Technology. Third Edition. Vol. 5. Grayson, M., Ed. John Wiley and Sons, New York, 1979a, pp. 773-785.

Johnson, P.R. Neoprene. In: Kirk-Othmer Encyclopedia of Chemical Technology. Third Edition. Vol. 8. Grayson, M., Ed. John Wiley and Sons, New York, 1979b, pp. 515-534.

Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. Eighth Edition. Vol. III. Van Nostrand Reinhold, New York, NY, 1992.

Li, S., Q. Dong, Y. Liu, and Y. Liu. Epidemiologic Study of Cancer Mortality Among Chloroprene Workers. Biomed. Environ. Sci. Vol. 2, 1989, pp. 141-149.

Lynch, M.A. Personal communication (letter dated October 24, 1997) from M.A. Lynch, Project Manager, DuPont Dow Elastomers L.L.C., Pontchartrain Site, LaPlace, LA, to C.W. Jameson, NTP Report on Carcinogens Project Officer, National Toxicology Program, Research Triangle Park, NC, 1997.

McAllister, R., E. Bowles, J. DeGarmo, J. Rice, R.F. Jongleux, R.G. Merrill, Jr., and J. Bursey. 1990 Urban Air Toxics Monitoring Program. EPA-450/4-91-024. U.S. Environmental

Protection Agency, Office of Air Quality Planning Standards, 1991, 281 pp.

NIOSH. National Institute for Occupational Safety and Health. National Occupational Exposure Survey (1981-83). Unpublished provisional data as of 7/1/90. Cincinnati, OH: Department of Health and Human Services, 1990.

NTP. National Toxicology Program. Technical Report Series No. 467. Toxicology and Carcinogenesis Studies of Chloroprene (CAS No. 126-99-8) in F344/N Rats and B6C3F$_1$ Mice (Inhalation Studies). NIH Publication No. 98-3957. 371 pp. National Toxicology Program, Research Triangle Park, NC, 1998.

Pell, S. Mortality in Workers Exposed to Chloroprene. J. Occup. Med. Vol. 20, 1978, pp. 21-29.

SRI. Directory of Chemical Producers, United States, 1996. Stanford Research Institute, Menlo Park, CA: SRI International, 1996.

Tice, R., R. Boucher, C. Luke, D. Paquette, R. Melnick, and M. Shelby. Chloroprene and Isoprene: Cytogenetic Studies in Mice. Mutagenesis Vol. 3, 1988, pp. 141-146.

TRI95. Toxic Chemical Release Inventory 1995. Data contained in the Toxic Chemical Release Inventory (TRI). Available from National Library of Medicine's TOXNET system, 1997.

TRI99. Toxic Chemicals Release Inventory 1999. Data contained in the Toxic Chemical Release Inventory (TRI). Available from the U.S. Environmental Protection Agency Office of Environmental Information, http://www.epa.gov/triexplorer/reports.htm, 2001.

Westphal, G.A., M. Blaszkewicz, M. Leutbecher, A. Müller, E. Hallier, and H.M. Bolt. Bacterial Mutagenicity of 2-Chloro-1,3-butadiene (Chloroprene) Caused by Decomposition Products. Arch. Toxicol. Vol. 68, 1994, pp. 79-84.