Chloroprene (2-Chloro-1,3-Butadiene)

126-99-8

Hazard Summary

Symptoms reported from acute (short–term) human exposure to high concentrations of chloroprene include giddiness, headache, irritability, dizziness, insomnia, fatigue, respiratory irritation, cardiac palpitations, chest pains, nausea, gastrointestinal disorders, dermatitis, temporary hair loss, conjunctivitis, and corneal necrosis. Symptoms of chronic (long–term) exposure in workers were fatigue, chest pains, giddiness, irritability, dermatitis, and hair loss. Chronic occupational exposure to chloroprene vapor may contribute to liver function abnormalities, disorders of the cardiovascular system, and depression of the immune system. Occupational studies have found that exposure to chloroprene increases the risk of liver cancer. Studies in animals have found an increased risk of tumors in multiple organs. The EPA has classified chloroprene as likely to be carcinogenic to humans.

Please Note: The main source of information for this fact sheet is the EPA's *Toxicological Review of Chloroprene* (1), which contains information on the carcinogenic and noncarcinogenic effects of chloroprene including the unit cancer risk (URE) and the reference concentration (RfC) for chronic inhalation exposure.

Uses

• Chloroprene is a flammable liquid with a pungent odor. It is used primarily in the manufacture of polychloroprene (Neoprene TM, duprene) which is a polychloroprene elastomer that is used to make diverse products including adhesives, automotive and industrial parts (e.g., belts and hoses), wire and cable covers, adhesives, caulks, flame-resistant cushioning and other applications requiring chemical, oil, and/or weather resistance. (1,3)

Sources and Potential Exposure

- Exposure to chloroprene is primarily occupational. Workers may be occupationally exposed to chloroprene by inhalation or dermal exposure. (1)
- The release of chloroprene to the environment may occur during its manufacture, transport, and storage and during the manufacture of polychloroprene elastomers and polychloroprene containing products. (2)

Assessing Personal Exposure

• No information was located regarding the measurement of personal exposure to chloroprene.

Health Hazard Information

Acute Effects:

- Symptoms reported from acute human exposure to high concentrations of chloroprene include giddiness, headache, irritability, dizziness, insomnia, fatigue, respiratory irritation, cardiac palpitations, chest pains, nausea, gastrointestinal disorders, dermatitis, temporary hair loss, conjunctivitis, and corneal necrosis. (1)
- Acute exposure may: damage the liver, kidneys, and lungs; affect the circulatory system and immune system; depress the central nervous system (CNS); irritate the skin and mucous membranes; and cause dermatitis and respiratory difficulties in humans. (1)
- High level exposures affected the liver, lungs, kidneys, and CNS in animals exposed by inhalation, gavage, or injection. Acute oral exposure of rats caused: inflammation of the mucous membranes; damage to the lungs, liver, spleen, and kidneys; and irritation of the gastrointestinal tract. (1)

Chronic Effects (Noncancer):

- Chloroprene has been reported to cause respiratory, eye and skin irritation, chest pains, temporary hair loss, neurological symptoms (e.g., dizziness, insomnia, headache), and fatigue in occupationally exposed workers. (1)
- Effects to the cardiovascular system (rapid heartbeat, reduced blood pressure) and changes in blood cell parameters (red blood cells, hemoglobin content, white blood cells, and platelets) have also been reported in occupationally exposed workers. (1)
- In animals, toxicity in multiple organ systems, including in the respiratory tract, kidney, liver, spleen, and forestomach, has been reported in chronic inhalation studies. (1)
- The Reference Concentration (RfC) for chloroprene is 0.02 milligrams per cubic meter (mg/m³). The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (1)
- The <u>RfC</u> for chloroprene was identified based on consideration of sensitive cellular effects observed in the nose, lung, and blood of male and female rats and female mice, respectively. (1)
- EPA has high confidence in the study on which the RfC was based because it was a well-designed study using two test species (rats and mice) with 50 animals per dose group. EPA has medium-to-high confidence in the overall database because the database contains several chronic inhalation studies in three species, well-designed embrytoxicity, teratological, and reproductive toxicity studies, and subchronic and chronic studies observing potential neurotoxic and

immunotoxic effects. A major limitation in the database is the lack of a complete two-generation reproductive toxicity study. As a result, EPA has medium-to-high confidence in the RfC. (1)

• EPA has not established a Reference Dose (RfD) for chloroprene. (1)

Reproductive/Developmental Effects:

- A study reported functional disturbances in spermatogenesis in workers exposed to chloroprene and increased spontaneous abortions in the wives of exposed workers. However, insufficient details are available in the reports to adequately evaluate the results. (1)
- Reproductive effects, including a decreased number of spermatogonia, a decline in sperm motility, an increased number of dead sperm, and degeneration of the testes, have been observed in male rats exposed by inhalation or dermal contact. (1)
- Increased embryonic mortality and decreased fetal weight were reported in rats exposed by inhalation, although contamination may have occurred during this study. (1)
- No effects on embryonic or fetal survival nor incidence of soft tissue or skeletal defects were observed in other studies of rats exposed by inhalation. (1).

Cancer Risk:

- Four occupational epidemiological studies reported statistically significant associations (two-to five-fold increased risk) between chloroprene exposure and liver/biliary passage cancer. A few epidemiological studies reported a non-statistically significant increased risk of lung cancer incidence and mortality associated with chloroprene exposure. (1)
- An inhalation bioassay by the National Toxicology Program (NTP) showed clear evidence of carcinogenic activity in both rats and mice, based on increased incidences of neoplasms of the oral cavity, thyroid gland, lung, kidney, liver, skin, mammary glands, and other organs. (1)
- EPA has classified chloroprene as likely to be carcinogenic to humans based on: 1) statistically significant and dose-related information from the chronic NTP bioassay showing the early appearance of tumors, development of malignant tumors, and the occurrence of multiple tumors within and across animal species; 2) evidence of an association between liver cancer risk and occupational exposure to chloroprene; 3) suggestive evidence of an association between lung cancer risk and occupational exposure; 4) proposed mutagenic action of chloroprene; and 5) structural similarities between chloroprene and the known human carcinogens, butadiene and vinyl chloride. (1)
- EPA additionally concludes that the weight of evidence supports a mutagenic mode of action for chloroprene carcinogenicity. (1)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of $3 \times 10^{-4} \, (\mu g/m^3)^{-1}$ for chloroprene based on tumor incidence in multiple organ systems of mice and rats. Taking into account the mode of action conclusion, EPA estimates that, if an individual were to continuously breathe air containing chloroprene at an average of $0.002 \, \mu g/m^3 \, (2 \times 10^{-6} \, mg/m^3)$ over his or her entire lifetime, that person would theoretically have no more than a one–in–a–million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing $0.02 \, \mu g/m^3 \, (2 \times 10^{-5} \, mg/m^3)$ would result in not greater than a one–in–a–hundred thousand increased chance of developing cancer, and air

containing 0.2 μ g/m³ (2 x 10⁻⁴ mg/m³) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (1)

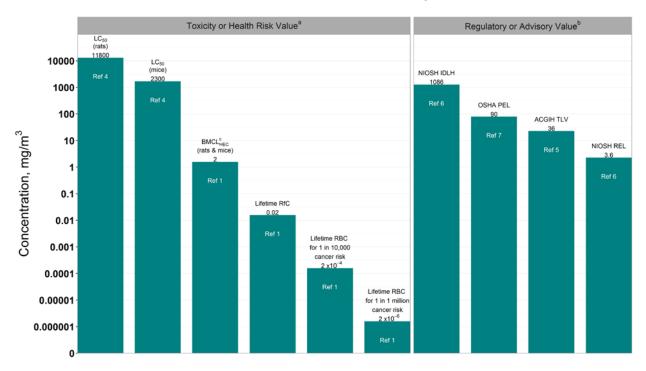
Physical Properties

- The chemical formula for chloroprene is C₄H₅Cl, and its molecular weight is 88.54 g/mol. (4,5)
- Chloroprene occurs as a colorless, mobile, flammable, and volatile liquid that is slightly soluble in water. (1,3)
- Chloroprene has a pungent odor, with an odor threshold of 0.4 mg/m³. (3)
- The vapor pressure for chloroprene is 188 mm Hg at 20 $^{\circ}$ C, and its log octanol/water partition coefficient (log K_{ow}) is 2.2. (1, 3)

Conversion Factors:

To convert concentrations in air (at 25 °C) from ppm to mg/m^3 : $mg/m^3 = (ppm) \times (molecular weight of the compound)/(24.45)$. For chloroprene: 1 $ppm = 3.62 \ mg/m^3$.

Health Data from Inhalation Exposure



ACGIH TLV— American Conference of Governmental and Industrial Hygienists' threshold limit value, which is a time-weighted average for chloroprene. It is the concentration for a conventional 8-hour workday and a 40-hour workweek, to which it is believed that nearly all workers may be repeatedly exposed, day after day, for a working lifetime, without adverse effect.

BMCL_{HEC} --Benchmark Dose Concentration Lower Confidence Limit - Human Equivalent Concentration.

LC₅₀ (Lethal Concentration₅₀)—A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

NIOSH IDLH—National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

NIOSH REL—NIOSH's recommended exposure limit, which is a ceiling for chloroprene. It is the concentration of chloroprene should not be exceeded during a 15-minute exposure.

OSHA PEL—Occupational Safety and Health Administration's permissible exposure limit expressed as a time—weighted average. It is the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-hour workday or a 40-hour workweek.

RBC (Cancer risk-based concentration)—A calculated concentration of a chemical in air to which continuous exposure over a lifetime is estimated to be associated with a risk of contracting cancer not greater than the specified probability (e.g., 1 in a million). The RBCs for chloroprene in the above graph are calculated using age-dependent adjusted factors (ADAFs).

- ^a Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
- ^b Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.
- ^c The BMCL is the statistical lower confidence limit on the concentration at the benchmark concentration, which is the concentration in human concentration terms, that produced a specified change in a response rate that is considered a critical effect. The BMCL was used as the point of departure for the RfC derivation. Three BMCL values including those for increased incidence in olfactory atrophy, alveolar hyperplasia and splenic hematopoietic cell proliferation in male F344/N rats, female F344/N rats, and female B6C3F1 mice, respectively, were identified as co-critical. After rounding to one significant figure, the individual BMCLs resulted in a similar value of 2 mg/m³. (1)

Summary created in April 1992, updated in September 2016

References

- U.S. Environmental Protection Agency. Toxicological Review of Chloroprene (CAS No. 126–99–8). In Support of Summary Information on the Integrated Risk Information System. September 2010.
 - http://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/1021tr.pdf
- 2. International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Some Monomers, Plastics and Synthetic Elastomers, and Acrolein. Volume 19. World Health Organization, Lyon. 1979.
- 3. Richard P. Pohanish, Editor. Sittig's Handbook of Toxic and Hazardous Chemicals and Carcinogens. 6th ed. Elsevier Publications, Oxford, UK. 2012.

- 4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
- 5. American Conference of Governmental Industrial Hygienists (ACGIH). 2015 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices. Cincinnati, OH. 2015.
- 6. National Institute for Occupational Safety and Health (NIOSH). Pocket Guide to Chemical Hazards. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 2015. http://www.cdc.gov/niosh/npg/.
- 7. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. Code of Federal Regulations. 29 CFR 1910.1000. 1998. Available at https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=100 99.