

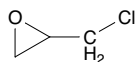
Epichlorohydrin

CAS No. 106-89-8

Reasonably anticipated to be a human carcinogen

First listed in the *Fourth Annual Report on Carcinogens* (1985)

Also known as 1-chloro-2,3-epoxypropane or CEP



Carcinogenicity

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

Cancer Studies in Experimental Animals

Epichlorohydrin caused tumors in two rodent species, at several different tissue sites, and by several different routes of exposure. In male rats, administration of epichlorohydrin by stomach tube caused benign and malignant tumors of the forestomach (carcinoma and papilloma), and inhalation exposure to epichlorohydrin caused benign and malignant tumors of the nasal cavity (carcinoma and papilloma). In female mice, epichlorohydrin administered by subcutaneous injection caused cancer at the injection site (sarcoma). Epichlorohydrin applied to the skin acted as an initiator in a tumor initiation-promotion study in female mice, but did not cause tumors when applied alone (IARC 1976).

Since epichlorohydrin was listed in the *Fourth Annual Report on Carcinogens*, additional studies in rodents have been identified. Administration of epichlorohydrin by stomach tube caused cancer of the forestomach (carcinoma) in rats of both sexes (Wester *et al.* 1985, IARC 1999). In male strain A/J mice (a strain with a high spontaneous incidence of lung cancer), epichlorohydrin administered by intraperitoneal injection increased the number of lung tumors per animal (Stoner *et al.* 1986, IARC 1999).

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to epichlorohydrin. One cohort study of workers exposed to epichlorohydrin at two factories found a significant excess of respiratory cancer; however, some of the workers had been engaged in the manufacture of isopropyl alcohol and may have been exposed to diisopropyl sulfate (Enterline 1982, IARC 1982).

Since epichlorohydrin was listed in the *Fourth Annual Report on Carcinogens*, the International Agency for Research on Cancer has reviewed its carcinogenicity twice (IARC 1987, 1999). The 1999 review included a follow-up study of the cohort exposed to epichlorohydrin and isopropyl alcohol (Enterline 1982), as well as additional cohort and nested case-control studies. No excess of lung cancer was observed in the follow-up study (Tsai *et al.* 1996), in a small cohort of workers exposed to epichlorohydrin and allyl chloride (Olsen *et al.* 1994), or in a nested case-control study of male chemical workers (Bond *et al.* 1986). A cohort study of resin and dye makers found a significant excess of lung cancer, but a nested case-control study of lung cancer in this cohort found no association with exposure duration or cumulative exposure level (Delzell *et al.* 1989). A nested case-control study of nervous-system cancer in the same cohort found a statistically nonsignificant excess of central nervous system cancer; risk increased with both exposure duration ($P_{\text{trend}} = 0.11$) and cumulative exposure level ($P_{\text{trend}} = 0.08$). These studies were limited by small

sample sizes, co-exposure of workers to other substances, and lack of control for potentially confounding variables. IARC (1999) concluded that there was inadequate evidence in humans for the carcinogenicity of epichlorohydrin.

Properties

Epichlorohydrin is an epoxide with bifunctional alkylating activity which at room temperature exists as a colorless liquid with a sweet, pungent, chloroform-like odor. It is soluble in water and benzene, miscible with ethanol, diethyl ether, chloroform, trichloroethylene, and carbon tetrachloride, and immiscible with petroleum hydrocarbons (IARC 1999). Epichlorohydrin is stable at normal temperature and pressure, but is highly flammable with moderate heating (Akron 2009). It can react violently with chemicals carrying an active hydrogen atom, including water (IARC 1999, HSDB 2009). It is heavier than air and may travel from its source and collect in low-lying areas (HSDB 2009). Physical and chemical properties of epichlorohydrin are listed in the following table.

Property	Information
Molecular weight	92.5 ^a
Specific gravity	1.18 at 25°C/4°C ^a
Melting point	-26°C ^a
Boiling point	118°C ^a
Log K_{ow}	0.45 ^a
Water solubility	66 g/L at 25°C ^b
Vapor pressure	16.4 mm Hg at 25°C ^a
Vapor density relative to air	3.3 ^a

Sources: ^aHSDB 2009, ^bChemIDplus 2009.

Use

Epichlorohydrin is used in the production of numerous synthetic materials, including epoxy, phenoxy, and polyamide resins, polyether rubber used in car parts, synthetic glycerin, glycidyl ethers, polythiols, elastomers, cross-linked food starch, surfactants, plasticizers, dyestuffs, pharmaceutical products, oil emulsifiers, lubricants, and adhesives (IARC 1976, WHO 1984). Epichlorohydrin may be used as a homopolymer or copolymer in the synthesis of epichlorohydrin rubber (Machine Design 2007). It is also used as a solvent for resins, gums, cellulose, esters, paints, and lacquers; to cure propylene-based rubbers; and in resins with high wet strength for the paper industry (IARC 1976, 1999). Epichlorohydrin is widely used as a stabilizer in chlorine-containing substances such as rubber, pesticide formulations, and solvents (HSDB 2009).

Production

Epichlorohydrin was first synthesized in 1854. Small-scale production in the United States began in 1937, and large-scale production in 1949. From 1973 to 1978, production ranged from 157 million kilograms (346 million pounds) to 250 million kilograms (551 million pounds) (IARC 1976, 1999). In 2009, epichlorohydrin was produced by 27 manufacturers worldwide, including 2 in the United States, 9 in East Asia, 6 in Europe, 8 in China, 1 in India, and 1 in the Middle East (SRI 2009), and was available from 50 suppliers, including 27 U.S. suppliers (ChemSources 2009). From 1989 to 2008, U.S. exports of epichlorohydrin ranged from a low of 15.8 million kilograms (34.8 million pounds) in 1992 to a high of 136 million kilograms (300 million pounds) in 2006; in 2008, exports were 81.9 million kilograms (180.6 million pounds) (USITC 2009). Over the same period, U.S. imports ranged from a low of 2.0 million kilograms (4.4 million pounds) in 1994 to a high of 19.1 million kilograms (42.1 million pounds) in 2000. Reports filed under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule from 1986

to 2002 indicated that U.S. production plus imports of epichlorohydrin totaled over 500 million pounds; in 1998, the reported quantity exceeded 1 billion pounds (EPA 2004).

Exposure

The routes of potential human exposure to epichlorohydrin are ingestion, inhalation, and dermal contact (HSDB 2009). Evidence suggests that epichlorohydrin is readily absorbed when ingested or inhaled and that it is a systemic poison when absorbed through the skin (WHO 1984). Exposure will occur primarily in occupational settings, but individuals in the general population may be exposed while using epoxy resins (Howard 1989) or through ingestion of food (WHO 1984, FDA 2010a,b,c,d,e). Food may contain epichlorohydrin as a result of its use as a cross-linker in modified food starch and in food processing or in food packaging materials, such as adhesives and coatings. Concentrations of epichlorohydrin in modified food starch are required to be below 0.3%, which limits the potential daily intake through ingestion.

According to EPA's Toxics Release Inventory, 45 facilities released a total of 155,878 lb of epichlorohydrin to the environment in 2007, of which 84% was released to air, 6% to surface water, and most of the remaining 10% to on- and off-site landfills (TRI 2009). Reported epichlorohydrin releases have declined continuously from a high of almost 909,000 lb in 1989, of which 77% was released to air, 1% to surface water, 22% to underground injection wells, and virtually none to landfills. Over time, the amount of epichlorohydrin released to land has increased, while total releases and releases to air have declined, and releases to surface water and underground injection wells have fluctuated. Epichlorohydrin has been detected, but not quantified, in surface water and river sediment (HSDB 2009). Epichlorohydrin was also released to the environment as a result of two railroad accidents in West Virginia; in 1963, 5,000 gal was released into the New River at South Fayette, and in 1978, 20,000 gal was released near the center of the town of Point Pleasant. In the latter instance, contamination of groundwater was confirmed; epichlorohydrin was found at a concentration of 75 ppm in the well closest to the spill site.

When released to air, epichlorohydrin will be degraded by photochemically produced hydroxyl radicals, with an estimated half-life of 4 days. If released to surface water, epichlorohydrin is expected not to adsorb to sediment, but to volatilize, with an estimated half-life of 19 hours in a model river and 12 days in a model lake (HSDB 2009). Hydrolysis is expected to occur with a half-life of 8.2 days in distilled water and 5.3 days in seawater. Hydrolysis will produce 3-chloro-1,2-propanediol in fresh water and 1,3-dichloro-2-propanol in seawater (Howard 1989). If epichlorohydrin is spilled on land, it most likely will volatilize or leach into the subsurface; biodegradation and hydrolysis also may occur in soil. Bioaccumulation in aquatic organisms is unlikely (HSDB 2009).

Occupational exposure may occur during the production of epichlorohydrin and during its use to synthesize end products. The National Occupational Hazard Survey (conducted from 1972 to 1974) estimated that 85,000 workers in 10 industry segments potentially were exposed to epichlorohydrin (NIOSH 1976), and the National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 80,170 workers in 24 industry segments, including 14,921 women, potentially were exposed (NIOSH 1990).

Studies of occupational exposure to epichlorohydrin have been conducted for the chemical and paper-manufacturing industries and at resin and synthetic leather manufacturing plants (Kuo *et al.* 2000, Luo *et al.* 2003, 2004, Korhonen *et al.* 2004). Comprehensive industrial surveys conducted for the National Institute for Occupational Safety and Health between 1973 and 1976 at seven facilities manufacturing epichlorohydrin, epoxy resins, and glycerol suggested that

chemical operators at these plants had the greatest potential for exposure to epichlorohydrin. Time-weighted-average (TWA) exposure concentrations ranged from less than 0.04 to 7.9 mg/m³. In two other epoxy resin manufacturing facilities, the TWA concentration of epichlorohydrin was generally below 3.8 mg/m³. Concentrations in the laboratory areas of these plants were higher, ranging from 3.8 to 18.9 mg/m³ (WHO 1984). In a solvent epichlorohydrin production plant, concentrations were as high as 5.5 ppm (20.8 mg/m³) during normal production and 54.9 ppm (207.5 mg/m³) when there were mechanical difficulties (Howard 1989). As of 2005, health hazard evaluations had been requested by workers in 10 facilities based at least in part on epichlorohydrin exposure; however, the NIOSH investigations resulted in a recommendation for workplace practice changes at only one facility (a wet corn milling facility), based on an epichlorohydrin concentration of 0.1 mg/m³ (Ferguson 1977, Lewis 1979, Markel 1979, Chrostek and Levine 1980, McGlothlin *et al.* 1980, Stephenson *et al.* 1981, Lee *et al.* 1982, Liss and Ruhe 1982, Lee 1985, Hills 1988).

Regulations

Coast Guard, Department of Homeland Security

Minimum requirements have been established for safe transport of epichlorohydrin on ships and barges.

Department of Transportation (DOT)

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

Environmental Protection Agency (EPA)

Clean Air Act

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

Prevention of Accidental Release: Threshold quantity = 20,000 lb.

Clean Water Act

Designated a hazardous substance.

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.

Reportable quantity (RQ) = 100 lb.

Threshold planning quantity (TPQ) = 1,000 lb.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of epichlorohydrin = U041, K017.

Listed as a hazardous constituent of waste.

Safe Drinking Water Act

Each public water system must certify annually that when epichlorohydrin is used in drinking water systems, the level does not exceed 0.01% dosed at 20 ppm (or equivalent).

Food and Drug Administration (FDA)

Food starch may be etherified or esterified by treatment with epichlorohydrin, with maximum epichlorohydrin levels ranging from 0.1% to 0.3% (depending on process).

Various epichlorohydrin copolymers may be used as food additives and food contact materials as prescribed in 21 CFR 172, 173, 175-178.

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) = 5 ppm (19 mg/m³).

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 0.5 ppm.

National Institute for Occupational Safety and Health (NIOSH)

Immediately dangerous to life and health (IDLH) limit = 75 ppm.

Listed as a potential occupational carcinogen.

Report on Carcinogens, Twelfth Edition (2011)

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