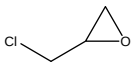
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	106-89-8
Chemical Name	1-Chloro-2,3-epoxypropane
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

In mammals, 1-chloro-2,3-epoxypropane (epichlorohydrin) was absorbed and metabolized rapidly after oral or inhalation exposure. The two primary routes of metabolism of epichlorohydrin were conjugation with glutathione (GSH) with subsequent metabolism to mercapturic acid conjugates that were eliminated in the urine, and hydrolysis of epichlorohydrin to α-chlorohydrin which was further metabolized and exhaled as CO_2 or excreted in urine as a mercapturic acid conjugate. In multiple investigations (oral and inhalation), approximately 25 to 42 percent was exhaled as CO_2 and roughly 50 percent was eliminated via the urine.

Acute oral LD_{50} values for epichlorohydrin in rats were 175 (female) and 282 (male) mg/kg and the dermal LD_{50} following a single occluded application to rabbits was 515 mg/kg. The acute inhalation LC_{50} for a 1-hour exposure of rats was 3617 ppm (13,746 mg/m^3) for males and 2165 ppm (8227 mg/m^3) for females (values for mice were similar). The LC_{50} for a 6-hour exposure of male rats was 360 ppm (1361 mg/m^3).

In primary irritation studies, epichlorohydrin was corrosive to the skin and eye. Vapors of epichlorohydrin at 1790 ppm or higher also produced damage to the cornea of rats. Epichlorohydrin was considered to be a skin sensitizer based on animal studies. In humans, epichlorohydrin was shown to be a severe irritant and a skin sensitizer.

Subchronic repeated-dose studies indicated that oral or inhalation exposure to epichlorohydrin caused local toxicity (irritation) at the site(s) of contact. Indications of systemic toxicity were principally changes in body weight and food consumption. Except at the site of contact, organ-specific toxicity was minimal for studies of 90 days or longer; increases in kidney weight accompanied by slight histopathological effects were observed at inhaled concentrations of 25 and 50 ppm (95 and 190 mg/m^3, respectively). The NOAEL for rats and mice following 90 days of exposure to epichlorohydrin vapors was 5 ppm (18.9 mg/m^3). The NOAEL for oral (gavage) dosing following 90 days of exposure was 1 mg/kg bw-day (based on decreases in red blood cell parameters and organ weight changes at higher doses). All of the repeated-dose studies confirm the irritant properties of epichlorohydrin, with localized irritation, often severe, occurring at the site of contact following repeated gavage dosing, at doses greater than approximately 1 mg/kg bw-day, and following inhalation exposure at concentrations greater than approximately 5 ppm (18.9 mg/m^3).

Epichlorohydrin was consistently genotoxic in both *in vitro* and *in vivo* assays.

Squamous cell carcinomas of the nasal epithelium in rats were observed following exposure via inhalation of epichlorohyrdin at the highest concentration of 30 ppm (113 mg/m^3). Squamous cell papillomas and carcinomas of the non-glandular stomach (forestomach) were observed in rats following gavage dosing with epichlorohydrin at the highest concentration of 10 mg/kg bw-day or following drinking water administration at 375 mg/L (approximately 18 mg/kg bw/day) or higher. Based on these findings, epichlorohydrin is considered to be carcinogenic in experimental animals. Carcinogenic effects in humans have not been established in the epidemiology studies of workers either manufacturing or using epichlorohydrin.

In an inhalation fertility study, male rats and rabbits were given doses of 5, 25, and 50 ppm (18.9, 95, and 190 mg/m^3, respectively) and mated with untreated females. Male rat infertility was observed at 50 ppm and preimplantation losses were observed at the two highest doses. The resorption rate was significantly increased at

50 ppm. These effects were reversed after 2 weeks of exposure. No effects on counts, motility, viability, and fertility of sperm were observed in the rabbits, nor were any effects observed on number of corpora lutea or resorptions in unexposed females mated to treated males. In a gavage study, male rats were treated with 12.5, 25, and 50 mg/kg bw/day and mated with untreated females. Fertility was assessed only at 50 mg/kg bw/day and was completely impaired. Several parameters related to sperm motility were affected at all doses with dose-dependent trends. Other oral studies also resulted in male infertility and effects on sperm at doses of 20 mg/kg bw/day and higher at exposures of one or more days; effects on fertility reversed in one of these studies, although two studies resulted in retained or abnormal sperm at 10 to 12 weeks after exposure ceased. Reproduction and fertility in female rats was not affected in inhalation and oral studies. Reproductive effects in humans have not been established in the epidemiology studies of workers either manufacturing or using epichlorohydrin.

Developmental toxicity studies were conducted by inhalation at doses of 2.5 and 25 ppm (9.5 and 95 mg/m^3) in rats and rabbits and via gavage at doses of 40, 80, and 160 mg/kg bw/day in rats and 80, 120, and 160 mg/kg bw/day in mice. In the gavage study in mice, epichlorohydrin resulted in decreased fetal body weights in mice (7 percent from controls at 120 mg/kg bw/day and 9 percent at 160 mg/kg bw/day). However, no other signs of fetal toxicity were observed in these studies.

Environment

Epichlorohydrin is a liquid with a melting point of -57 °C and boiling point of 116.4 °C. At 20 °C the density is 1.181 g/cm^3. The vapour pressure of epichlorohydrin is 22.7 hPa, while the water solubility is 66,000 mg/L at 25 °C. The measured log K_{ow} is 0.45.

The half-life for indirect photooxidation of epichlorohydrin in the atmosphere is 24 days. Based on Level III fugacity modeling, when released to air, epichlorohydrin will primarily remain in air with some transfer to water and soil. When released to water, epichlorohydrin will remain dissolved in water. When released to soil, epichlorohydrin will be primarily dissolved in soil pore water (groundwater). Simultaneous release to air, water and soil is predicted to result in distribution to water and soil compartments. A hydrolysis study (OECD TG 111) revealed half-lives in water of 7.3, 3.9 and 6.8 days at pH 4, 7 and 9 at 20 °C, indicating epichlorohydrin is hydrolyzed in the aquatic environment. Hydrolysis of epichlorohydrin results in the formation of 1-chloro-2,3-dihydroxypropane. Epichlorohydrin was 75% degraded in two days in a biodegradation assay with adapted sludge. On the basis of this study, epichlorohydrin can be considered to be biodegradable. Based on the low log K_{ow} of 0.45, the bioaccumulation potential is expected to be limited.

An acute fish toxicity test with juvenile fathead minnows revealed an LC_{50} of 10.6 mg/l (nominal concentration) after 96 hours of exposure. An acute toxicity test with water fleas (*Daphnia magna*) resulted in a 48-hour EC_{50} value of 23.9 mg/l based on nominal concentrations. An OECD guideline study with algae (*Pseudokirchneriella subcapitata,* formerly known as *Selenastrum capricornutum*) resulted in a 72-hour EC_{50} of 7.1 mg/l and a NOEC value of 1.7 mg/l, both based on biomass and mean measured concentrations. The 72-hour EC_{50} based on growth rate was 15 mg/l.

Exposure

The annual global production volume of epichlorohydrin is estimated to be about 1 million tonnes per year. The estimated production in the US for 2002 was 480 000 metric tonnes. Releases of epichlorohydrin to the environment from all industries in the United States have been reported as approximately 100 000 kg/year (~100 metric tonnes/year), most of which were released to the atmosphere. The estimated production in Europe for 2002 was 317 000 tonnes. The estimated production in Japan and the Pacific region for 2002 was 365 000 tonnes.

Epichlorohydrin is used only as a chemical intermediate (industrial use). It is used in closed systems with approximately 75% of world consumption of epichlorohydrin used for the production of epoxy resins and 9% used in the production of synthetic glycerin. The remainder is used for the production of miscellaneous products such as elastomers, polyamide-epichlorohydrin resins for wet-strength resin production, glycidyl ethers, glycidyl methacrylate, surfactants, ion exchange resins, polyamide water treatment chemicals, flame retardants and quaternary amines. In the occupational setting, closed system operations allow for the safe handling of epichlorohydrin and personal protective equipment is routinely suggested.

Consumer products are expected to contain only trace levels of epichlorohydrin based on its reactivity and use as an intermediate in polymer and other chemical synthesis since epichlorohydrin is not directly added to consumer

products. The World Health Organization derived a provisional drinking water guideline of 0.4 µg/L (2004). In the sponsor country from a preventive health standpoint, exposures follow the principle of as low as reasonably achievable (ALARA) preferably zero.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is a low priority for further work. The chemical possesses properties indicating hazards for human health (skin, eye, and respiratory tract irritation, skin sensitization, genetic toxicity, carcinogenicity, and reproductive effects). Based on data provided by the sponsor country (relating to production by several producers in the United States which account for 42 percent of the global production and relating to the use pattern primarily in the United States), risk management measures are being applied (engineering controls, occupational standards, drinking water standards, Material Safety Data Sheets, and other US regulations). Countries may desire to check their own risk management measures to find out whether there is need for additional measures.

Environment: The chemical has properties indicating a hazard for the environment (acute aquatic EC/LC50 values between 1 and 100 mg/l). However the chemical is of low priority for further work for the environment because environmental exposures are expected to be limited due to its use as a chemical intermediate in closed systems.