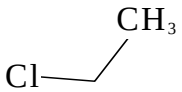
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	75-00-3
Chemical Name	Chloroethane
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Chloroethane is readily absorbed by the lungs. Following a single breath exposure, 30% of the administered radioactivity was eliminated on the breath within 1 hour in humans. 25% of the amount in the blood is localized in the plasma fraction, whereas 75% is found in the cellular fraction. Quantitative species differences were observed with regard to glutathione (GSH) conjugation and oxidation by cytochrome P-450 dependent monooxygenases pathways, revealing higher rates for mice compared to rats. Chloroethane exposure resulted in induction of cytochrome P-450 IIE1 (increase in p-nitrophenol hydroxylase activity) in mice and rats. In the urine of both species S-ethyl-N-acetyl-L-cysteine was detected, and was generally higher in mice than in rats. The non-acetylated S-ethyl-L-cysteine was excreted in mouse urine only. Exposure resulted in a GSH depletion of about 50 % in the lung and uterus of both species, whereas liver and kidney GSH concentrations were not dramatically affected. GSH transferases were not induced. At high exposure concentrations the oxidative pathway (P-450) is saturated and increasing amounts are metabolized via the GSH pathway. The kinetic behaviors for chloroethane metabolism in rats were a combination of saturable and first-order processes. The dechlorination rate for chloroethane under the experimental conditions was low (~ 0.5 %) and found to be inducible by phenobarbital and benzopyrene, but not methylcholanthrene. These results indicate a cytochrome-P-450 dependent enzymatic reaction. The metabolism of chloroethane by microsomes from rats and mice was decreased after pretreatment of animals with phenobarbital or 3-methylcholanthrene. Acetaldehyde was detected as a metabolite.

Chloroethane has been tested for acute toxicity by the inhalation route of exposure. The acute LC_{50} for rats and mice is greater than 19,000 ppm (50,000 mg/m^3). No clinical signs of toxicity were seen. Human exposure has shown that chloroethane vapor is irritating to the eyes, nose and throat. Chloroethane exposure to skin has also resulted in contact dermatitis. In humans, skin sensitization to chloroethane can also occur. In humans, narcosis occurring at very high concentrations was the basis of historic use as a surgical anesthetic.

Repeated dose toxicity studies with chloroethane have been conducted by the inhalation and oral routes of exposure. In general, no compound-related clinical signs or gross or microscopic pathologic effects were seen in any of the repeated dose inhalation studies with rats at concentrations up 10,000 ppm (26,000 mg/m^3). Decreased body weight (19000 ppm (50,000 mg/m^3) for 13 weeks) and slight but statistically significant increases in liver to body weight ratios was observed for male rats exposed to 4000 (10,470 mg/m^3) or 10000 ppm (26,000 mg/m^3) for 2 weeks. Similarly, no clinical signs of toxicity have been observed in mice exposed to chloroethane by inhalation up to 19,000 ppm (50,000 mg/m^3). An increase in liver weights (absolute and relative to body weight) was observed in some studies. In a 13 week study the liver weight to body weight ratio for female mice exposed to 19000 ppm (50,000 mg/m^3) was significantly greater than that for controls, but no microscopic liver changes were observed. An increase in the mean liver weights of both male and female mice exposed to 5000 ppm (13,088 mg/m^3), 23 hrs/d for 11 days. Pathological examination revealed an increased liver size in two males and one female exposed to 5000 ppm. A minimal increase in the degree of hepatocellular vacuolization in four of seven mice/sex exposed to 5000 ppm was observed, with a LOAEL of 5000 ppm. Similar effects on the liver were not noted in the remaining studies. Repeated inhalation exposure of chloroethane by rabbits or beagle dogs did not result in the observation of any treatment related effects. NOAELS were 9620 ppm (25.4 g/m^3) (rabbit) and 10,000 ppm (26,000 mg/m^3) (beagle dogs). There were no treatment related effects in rats and rabbits exposed to chloroethane by the oral route.

Chloroethane induced gene mutations *in vitro* in both bacterial and mammalian systems, with and without metabolic activation. However, in a mouse micronucleus assay, chloroethane did not induce chromosomal damage *in vivo* at concentrations as high as 25,000 ppm (65,440 mg/m^3) and no consistent increase in S-phase DNA synthesis and had no genotoxic activity in a UDS assay. The *in vitro* genotoxicity of chloroethane has not been demonstrated *in vivo,*

There was clear evidence of carcinogenicity for female mice. There was equivocal evidence of carcinogenic activity of chloroethane for male and female rats. A study in male B6C3F1 mice was considered to be inadequate.

There were no compound-related reproductive effects of rats or mice exposed to 15,000 ppm (39,264 mg/m^3) for up to two years (NOAEL = 15,000 ppm). Mice exposed to up to 15000 ppm (39,264 mg/m^3) chloroethane for 14 consecutive days had significantly longer estrous cycle duration than the pre-exposure duration for the same group and for the corresponding controls; the effect was attributed to a general stress response (NOAEL = 15,000 ppm). However, a direct exposure-related effect of chloroethane on neuroendocrine function cannot be excluded. Developmental toxicity (delayed ossification and supernumary ribs) was observed in mice when exposed at 5000 ppm (13,088 mg/m^3) chloroethane vapor for 6 h/d on days 6 through 15 of gestation. The NOAEL for maternal and teratogenicity were >5000 ppm. Weak evidence of developmental toxicity was manifested by very slight fetotoxicity at high concentrations.

Environment

The melting point of chloroethane is -138.7°C and the boiling point is 12.3 °C at 1013 hPa. The vapor pressure is 1347 hPa at 20 °C. The water solubility of chloroethane is 5.74 g/L (20 ^{o}C) and the calculated log Kow is 1.43. The Henry's Law Constant is 1.1 x 10^{-2} atm-cu m/mole.

Chloroethane has an estimated atmospheric half-life (hydroxyl radical oxidation) range of 26.5 to 66.8 days. The hydrolysis half-life is estimated to range between 38 days and 2.6 years. Ethanol and HCl are the hydrolysis products. Results of Mackay Level I distribution modeling at steady state show that chloroethane will partition primarily to the air compartment (99.8%), with a negligible amount partitioning to water (0.19%) and soil (0.01%). Level III modeling using loading rates for air, soil and water of 1000 kg/h predicted the following distribution: air (49.4 %) water (47.3 %), soil (3.2 %) and sediment (0.04%). Using the Henry's Law constant, the volatilization half-lives for a model river and model lake are 50 hours and 3.2 days, respectively. Biodegradation studies suggest that chloroethane is not biodegradable. The calculated BCF is 2.5.

The 96-hour LC_{50} for bluegill (*Lepomis macrochirus*) exposed to chloroethane under static conditions was 2250 mg/L (measured). Similar results were obtained with largemouth bass (*Micropterus salmoides*), with an LC_{50} greater than 2000 mg/L (measured). The 48-hour EC_{50} for *Daphnia magna* exposed to chloroethane was 58 mg/L (measured). The 72-hour ErC_{50} (growth rate) for *Scenedesmus subspicatus* exposed to chloroethane was 11.8 mg/L (measured). The 72-hour E_bC_{50} (biomass) for *Scenedesmus subspicatus* was 39 mg/L (measured). Chloroethane possesses properties indicating a hazard for the environment (acute toxicity to invertebrates and algae). However, its volatility and limited potential for bioaccumulation limit the potential for hazard to the environment.

Exposure

In recent years, two previous end uses of chloroethane (i.e. manufacture of tetraethyl lead which was used as an additive anti-knock agent in gasoline, and use as a foam blowing agent) have largely been eliminated in the Sponsor Country. These data show that nearly all of the chloroethane produced for the current US markets goes into consumptive uses, i.e. uses where the chloroethane is a feedstock used to produce different end product chemicals. Only a small volume goes into emissive uses such as foam blowing (2%).

In 2004, 31,624 tonnes of chloroethane were produced in the United States at the only manufacturing site. In production, this material is handled in closed systems. Engineering controls during production include proper ventilation, containment, safety equipment and actual hardware designed to minimize exposure, through splashing, or exposure to the air. Transfer of this material is in closed pipe systems rather than in open systems to minimize loss of this material (volatilization). At the production site, approximately 175 workers have potential exposure to chloroethane, with measured levels in the range of 0-5 ppm. Chloroethane is transported from the production site to the industrial consumer primarily for consumptive uses. According to information in the USEPA Toxic Release Inventory data base for 2003, chloroethane use was reported at 44 sites, with total reported emissions of 781,700 lbs. (355 tonnes). Changes in end uses have significantly reduced emissions, e.g. in 1989 (a year with typical past end

use activities) 50 sites reported total emissions of 5,200,000 lbs. (23,587 tonnes). In 2003 only one site, where it was used in foam blowing, reported emissions over 100,000 lb/year, whereas the majority of the individual sites (25/44) reported total emissions of less than 1000 lb/year. The American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) Time Weighted Average (TWA) for chloroethane is 100 ppm (264 mg/m^3) and the US Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) is 1000 ppm (2640 mg/m^3) TWA . The USEPA regulates chloroethane under both the Clean Air Act as amended in 1990, Sec. 112 (b)(1) (listed as hazardous air pollutant) and the Clean Water Act (designated as hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act). Chloroethane is not used in consumer products. Environmental exposure to chloroethane can occur from fugitive and stack emissions at use sites and from its use in foam blowing.

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

Human Health: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for human health (skin sensitisation, genotoxicity *in vitro* which has not been demonstrated *in vivo*, clear evidence of carcinogenicity in female mice and equivocal evidence in rats, weak evidence of developmental toxicity in mice as manifested by very slight fetotoxicity at high concentrations). Based on data presented by the Sponsor country, relating to production volume in one member country, which accounts for an unknown fraction of global production, and relating to the use pattern in several OECD countries, exposure to humans is expected to be low. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for the environment (acute toxicity to invertebrates and algae). However, the chemical is of low priority for further work for the environment because of its volatility and limited potential for bioaccumulation.