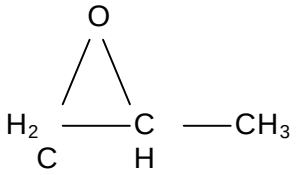
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	75-56-9
Chemical Name	Methyl oxirane (Propylene oxide)
Structural Formula	

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The human health effects database meets the requirements for the SIDS data package. Propylene oxide is extremely flammable. Hazardous polymerisation may occur when in contact with highly active catalytic sources or changes of neutrality (e.g. in contact with acids, bases, oxidising materials).

PO is rapidly absorbed into the tissues and metabolised via conjugation with glutathione and hydrolysis. At high doses saturation of the metabolic process for elimination is assumed. Haemoglobin and DNA adduct formation has been observed in several animal tissues following inhalation exposure, including nasal mucosa, trachea, lung, liver, brain and testes. The presence of kidney adducts have not been investigated in the inhalation experiments. PO is harmful to human health following single exposure via inhalation, ingestion or contact. No reliable human data are available. In experimental animals, acute toxicity oral LD50 values are 520 - 950 mg/kg; dermal LD50s values are 1250mg/kg and 950 mg/kg; inhalation 4 hour LC50 values are about 4000 ppm in the rat and 1740 ppm in the mouse. Signs of respiratory tract irritation were observed.

PO may cause local irritation on contact with the skin and eyes. PO has demonstrated some potential to cause skin sensitisation and it is plausible that it could bind to tissue proteins and elicit an immunological response. There is no data available on respiratory sensitisation. Repeated inhalation exposure produces irritation of the nasal epithelium, with marginal effects at 30 ppm and pronounced epithelial damage at 100 ppm and above. Neurotoxicity was observed in experimental animals exposed to 1500 ppm for 7 weeks, although no such effects were observed in rats exposed to 300 ppm for 24 weeks. Repeated oral administration caused gastric irritation, with microscopic changes such as reactive changes in the squamous epithelium of the stomach at the lowest dose tested, 15 mg/kg. Target tissues are the sites of the initial contact.

Propylene oxide is a direct acting mutagen in a wide variety of standard *in vitro* test systems and genotoxic in somatic cells *in vivo*. There is no evidence for propylene oxide induced heritable mutations in germ cells from dominant lethal tests in rats and mice. Given that propylene oxide is a direct-acting mutagen that might reach the germ cells (DNA adducts seen in the testes) the possibility for PO inducing heritable mutations in germ cells cannot be discounted.

PO is a respiratory tract carcinogen in animals. Repeated gavage induced forestomach carcinoma in rats. At present, the relative contribution to the carcinogenic process made by irritation, consequential proliferative response and genotoxicity is unclear.

There is no evidence for reproductive and developmental toxicity at non-maternally toxic dose levels from animal studies.

Environment

The environmental effects database meets the requirements for the SIDS data package.

Short-term toxicity data are available for fish, daphnia and algae, but there are no long-term studies. Fish appear to be the most sensitive organisms, with the lowest 96h LC_{50} value of 52 mg/l for rainbow trout, *Oncorhynchus mykiss*. The only reported test on aquatic invertebrates was conducted on *Daphnia magna*, 48-hour EC_{50} 350 mg/l. A single algal test is available, with 96h EC50 240 mg/l, NOEC 100 mg/l based on growth (*Selenastrum capricornutum)*. A PNEC of 52 µg/l was derived from the acute fish toxicity data, using an assessment factor of 1000 according to the EU technical guidance. There are no data on sediment organisms, so the equilibrium partitioning method was used to obtain a PNEC of 43.2 µg/kg for sediment. There are some data on effects on soil from fumigation experiments using high exposure levels. These demonstrate that propylene oxide sterilises soil. However, these results could not be used to derive a NOEC. The equilibrium partitioning method was used to derive a PNEC for soil of 16.5 µg/kg. Data relating to terrestrial plants are also available. The germination and growth of wheat and alfalfa were retarded by 50-60% in propylene oxide-treated soil (initial concentration 32 and 68 g propylene oxide /kg dry weight).

Propylene oxide is not considered to be important as a cause of photochemical air pollution. Although some of the potential products of propylene oxide breakdown in the atmosphere have relatively high photochemical ozone creation potentials, they are unlikely to be formed at a rate that could give rise to local air pollution problems.

Exposure

The annual world production of propylene oxide (PO) was 3.5 million tonnes in 1990 with an increasing trend. Production in the European Union (EU) is estimated as 1.45 million tonnes, with 1.5 million tonnes used. There are at least 7 EU producers and an estimated 150-300 user plants within the EU. Propylene oxide has two main use areas: as a monomer in polymer production (polyols, used in polyurethane production and other areas) and as an intermediate (for propylene glycol, propylene glycol ethers, butanediol). Direct uses include use as a stabiliser (e.g. in dichloromethane and other hydrocarbons), fumigation of foodstuffs (in the USA) and as a solvent in the preparation of samples for electronmicroscopy. Propylene oxide is not used as a food fumigant in the EU and this has not been addressed in the accompanying risk assessment. Release of propylene oxide to water and air compartments could arise from production and processing, and there is possible release to air arising from direct use.

In the EU, during manufacture and use as an intermediate PO is mainly used in closed systems and there is a potential for occupational exposure to occur via inhalation or contact during breaches of the system. The potential for exposure is controlled to as low as is reasonably practicable. This includes use of enclosed sampling systems, dry break coupling systems for transfer of PO to or from rail and road tankers, magnetic delivery pumps, systems for purging and testing process lines before breaching, use of PPE and the monitoring and control of fugitive emissions. PO is used as an intermediate in the manufacture of consumer products. Because of the reactivity of PO and subsequent dilution in consumer products, consumer exposure to residual PO in consumer products (foodstuffs, medicinal products, and hydraulic brake fluids for cars) is considered to be extremely low. Human exposure indirectly via the environment is primarily via inhalation and is extremely low.

Propylene oxide is a liquid, with a melting point of -112.16°C, boiling point of 34°C, vapour pressure 60 kPa at 20°C, water solubility 400 g/l and octanol-water partition coefficient (log Kow) 0.055. The half-life in air is estimated as 32 days. The substance hydrolyses in water, with a half-life at neutral pH of 22 days. The hydrolysis product is propylene glycol which is readily degradable. The biodegradation data shows variable results; it has been

interpreted as showing inherent biodegradability but with ready biodegradation in wastewater treatment plants where bacterial populations are acclimated. Propylene oxide is not very volatile from water (a Henry's Law constant of 12.4 Pa m^3 $mole^{-1}$ has been assumed) and has a high water solubility. It is unlikely to bioaccumulate, since the predicted log BCF is -0.65. Propylene oxide will not be sorbed strongly to organic matter (predicted Log Koc = 1.05).

NATURE OF FURTHER WORK RECOMMENDED

Sufficient information exists to address hazard classification for all SIDS endpoints and for other non-SIDS endpoints. However, the chemical is a candidate for further work as follows:

National or regional exposure information gathering and risk assessment may need to be considered where there is potential for exposure.

If significant soil exposure is likely, for example from fumigant use, it may be necessary to refine the PNEC for soil and soil toxicity testing may be required. It is noted that in the USA use as a fumigant is well controlled.

No thresholds have been identified below which there would be no concern for human health for the endpoints of mutagenicity and carcinogenicity (based on an existing regional risk assessment for Europe). In the EU, further risk reduction was not considered necessary as the industry currently maintains occupational exposures to be as low as is reasonably practicable (further information available from SIDS dossier). This conclusion is valid so long as industry continue to implement new procedures to reduce exposures when possible. It is noted that in the USA the minor fumigant use is highly controlled and regulated. Further risk reduction is not necessary for consumers or for exposures via the environment where exposure is extremely low. Due to insufficient information on skin sensitisation, a risk assessment was not conducted for this endpoint. Due to the concerns for mutagenicity and carcinogenicity (outlined above) further testing for this endpoint would not affect the risk assessment or management outcomes.