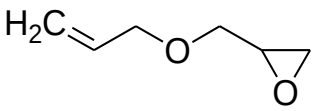
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	106-92-3
Chemical Names	Allyl 2,3-epoxypropyl ether
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

After i.p. injection in mice allyl glycidyl ether is partly metabolized by epoxidation and/or hydrolysis to diglycidyl ether, 1-allyloxy-2,3-dihydroxypropane and/or 2,3-dihydroxypropyl glycidyl ether.

The acute oral LD_{50}-value is between 260-340 mg/kg bw in mice and 1600 mg/kg bw in rats. Common clinical signs observed comprised distress such as lacrimation, dyspnea and depression. At necrospy, rats that died showed inflammation of the lungs and irritation of the gastroenteric tract. The acute inhalation LC_{50}-value is 1.26 mg/l in mice and 3.12-4.66 mg/l in rats. Considerable lacrimation, nasal and salivary discharge, dyspnea, gasping and corneal opacity were noted. At necrospy, rats that died showed moderate to severe diffuse inflammation and haemorrhage of the lungs. Allyl glycidyl ether is less toxic dermally. Varying degrees of skin irritations were observed. The LD_{50} is 2550 mg/kg bw in rabbits.

Based on tests with rabbits, allyl glycidyl ether is a skin and severe eye irritant. Based on results from several acute and repeated dose inhalation studies in rat and mice and a respiratory irritation study in mice, allyl glycidylether can be concluded to be a respiratory tract irritant.

No animal tests for sensitisation are available. However, several human case reports indicate that allyl glycidyl ether has potential for skin sensitization.

In several repeated inhalation studies exposure to allyl glycidyl ether revealed effects on body weight gain as well as the respiratory tract (nasal passage), which can be attributed to its irritating properties, at all dose levels. The 14-day NOAEL for inhalation toxicity in rats and mice is lower than 117 mg/m^3. The 90-day NOAEL for inhalation toxicity in rat and mice is lower than 19 and 4.7 mg/m^3, respectively. The 50-day NOAEL for inhalation toxicity in rats is lower than 1214 mg/m^3. The overall NOAEL for inhalation toxicity is set below 4.7 mg/m^3 based on the longest exposure period (90 days: 6h/day, 5 days/week) with mice where effects were seen on histopathology in the nasal passage, such as chronic inflammation of the mucosa and squamous metaplasia of the respiratory epithelium.

Allyl glycidyl ether is found to be mutagenic/genotoxic in all *in vitro* tests conducted (Ames, sister chromatid exchange assay and chromosome aberration test) with and without metabolic activation. Allyl glycidyl ether was positive in an *in vivo* mouse micronucleus test as well as *in vivo* drosophila sex-linked recessive lethal test. It is shown *in vitro* as well as *in vivo* that allyl glycidyl ether may form adducts to proteins. In addition, allyl glycidyl ether is capable of producing adducts of DNA *in vitro* and *in vivo* (N-7-guanine, N-1-adenine, N-3-adenine and N-3-cytosine, N-3-uracil) after dermal application and i.p. administration in mice. Based on these results, allyl glycidyl ether is an *in vitro* and *in vivo* genotoxicant.

Carcinogenicity was studied in lifetime inhalation studies in Osborne-Mendel rats and B6C3F1 mice (0, 23.3 and 46.6 mg/m^3). The biological significance of three neoplasms observed in the respiratory tract in male rats could not be assessed due to the lack of historical control data in this strain. The number of tumors in mice is limited, but the rarity of the neoplasms seen in this species and the presence of preneoplastic lesions at the site of the tumors suggests carcinogenic potential. Based on these studies and the demonstrated *in vitro* and *in vivo* genotoxicity allyl glycidyl ether is considered to have a carcinogenic potential.

An 8-week premating inhalation study was performed with both rats (0, 140, 467 and 934 mg/m^3 and mice (0, 19, 47, 140 mg/m^3). In mice, the parental NOAEL was 47 mg/m^3 based on decreased body weight gain in males and females. Fertility in mice was not affected up to the highest dose of 140 mg/m^3.
In rats however, inhalation of allyl glycidyl ether led to a markedly reduced fertility. The NOAEL for fertility is lower than 140 mg/m^3 based on the decreased pregnancy rate when males were exposed. Abnormal sperms are likely to be related to the reduced number of pregnancies. At 934 mg/m^3, the percentage of abnormal sperms was increased from 0.64% to 1.11%. Sperm related impairment of fertility is supported by testicular necrosis that was observed in rats after 4 consecutive intramuscular exposures to 400 mg/kg bw allyl glycidyl ether. A parental NOAEL was derived to be 140 mg/m^3 based on a decrease in body weight gain. A developmental toxicity study is not available. As it is considered that workplace exposure is well controlled there is no need for further testing.

Environment

Allyl glycidyl ether is a colorless liquid with a freezing point of -100°C, a boiling point of 154°C and a vapor pressure of 5.73 hPa (at 25°C). The substance has a high solubility in water of 128 g/l (at 20.2°C) and a log Kow of 0.34. A half-life for photo-oxidation by reaction with OH-radicals in air (1.5×10^6 OH/cm^3) of 3.25 hours has been calculated (AOPWIN v.1.91).

In a closed bottle test (OECD TG 301D) allyl glycidyl ether was not readily biodegradable. 5-9% of the test substance was degraded after 28d. Based on a GLP test according to OECD TG 111 , allyl glycidyl ether is not stable in water and is hydrolyzed within days to weeks, depending on pH conditions. A half-life of 243 hrs at pH 4, 324 hrs at pH 7, and 171 hrs at pH 9 was determined. 3-allyloxy-1,2-dihydroxy propane, which can be formed by opening of the epoxide ring, is expected to be the main hydrolysis product of allyl glycidyl ether. 3-allyloxy-1,2-dihydroxy propane was not readily biodegradable in an OECD 301C guideline test (47% degradation in 28 days) . No measured data on bioaccumulation are available for allyl glycidyl ether but the substance is not expected to bioaccumulate due to its low Kow. A BCF of 3.16 (log BCF = 0.5) was calculated with the BCFWIN program (v2.15).

Based on Level I fugacity modeling (EQC Level I, version 3.00) allyl glycidyl ether will partition primarily into water (90%) and air (9.5%). Level III fugacity modeling, assuming continuous discharge of the substance, loss by degradation and advection and non-equilibrium conditions between environmental compartments, indicates that 99.9% of allyl glycidyl ether will stay in water if released only into surface water. When released only into air, 44% will remain in air, 21% will partition to water, 35% to soil and only a negligible amount to the sediment. When released only to soil, 34% of allyl glycidyl ether will partition to water and 66% will remain in soil.

Aquatic testing has resulted in a 96-h LC_{50} in fish (*Cyprinus carpio*) of 36 mg/l, a 48-h EC_{50} in aquatic invertebrates (*Daphnia magna*) of 50 mg/l, and a 72-h EC_{50} in aquatic plants (*Pseudokirchneriella subcapitata*) of higher than 79 mg/l based on growth rate (72-h LC_{50} = 53 mg/l for biomass; NOEC = 20 mg/l for growth rate and biomass). No data on chronic toxicity to aquatic organisms are available for allyl glycidyl ether.

Exposure

Allyl glycidyl ether is used exclusively as an intermediate for synthesis, mainly of resins and other polymers. Total production volume is not known but the chemical is an HPV substance.
Allyl glycidyl ether is produced and used in closed systems (e.g. pipelines) or in semi-closed systems (e.g. manual filling of reactors). Exposure is thus expected to be minimal for workers. Available short-term occupational monitoring data at several sites indicate airborne concentrations below the detection limits of typically 1 mg/m^3. If emission occurs into the workplace atmosphere, appropriate protective equipments are in place (e.g. local exhaust ventilation and use of personal protective equipment such as full face mask, filter mask, gloves and dedicated clothing). Exposure

of the environment is considered to be low as well. Emission is mainly occurring from cleaning operations at the production sites. According to information from the Sponsor Country allyl glycidyl ether is not used in consumer products.

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

Human health:
The chemical is of low priority for further work. The substance possesses properties indicating a hazard for human health (skin and eye irritant, irritant to the respiratory tract, potential skin sensitizer, acute and repeated dose toxicity, genotoxicity, potential carcinogen, toxic to fertility). However, based on data presented by the Sponsor Country, relating to production by three producers in two countries, which accounts for an unknown fraction of global production, exposure to humans is anticipated to be low. Therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor Country.

Environment:
The chemical is of low priority for further work. The substance possesses properties indicating a hazard for the environment (acute toxicity to aquatic organisms between 1 and 100 mg/l). However, based on data presented by the Sponsor Country, relating to production by three producers in two countries, which accounts for an unknown fraction of global production, exposure to the environment is considered to be low. Therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor Country.