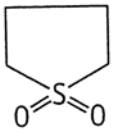
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	126-33-0
Chemical Name	Tetrahydrothiophene 1,1-dioxide
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

In rats dosed intravenously at 500 mg/kg, 28%, 36% and 37% of the dose was excreted unchanged between days 0-2, 0-4 and 0-7, respectively. At 1000 mg/kg, 50% and 67.2% of the dose was excreted unchanged between days 0-2 and 0-4, respectively. The observation that the proportion of the dose recovered increased with dosage suggests that the metabolic pathway is saturable. In rabbits, dogs and squirrel monkeys given a single iv injection, this chemical was rapidly distributed throughout the body and was slowly removed from plasma with a half-life of 3.5-5 hours. One major metabolite with 85% of the urinary radioactivity was found in male rats injected intraperitoneally with this chemical. In a follow up study, the metabolite was identified as 3-hydroxysulfolane in the urine of rabbits injected intraperitoneally with this chemical.

LD_{50} values by gavage [OECD TG 401] were 2006 mg/kg (males) and 2130 mg/kg (females) in rats. Dermal LD_{50} in male and female rats was greater than 2000 mg/kg [84/449/EEC, B3]. Inhalation LC_{50} in male and female rats(four hours) was greater than 12,000 mg/m^3. Acute behavioural studies in rats indicated that hypothermia contributed to the behavioural effect of an interperitoneal injection of 800 mg/kg of sulfolane. Rabbits became hyperthermic, at 28°C, upon subcutaneous injection of 600 mg/kg sulfolane.

The chemical is not irritating to guinea pig and rabbit skin or to rabbit eyes. The chemical was not sensitising (0/20) in a guinea pig maximisation test [84/449/EEC, B6].

In a 28 day repeat dose toxicity study [Japanese TG] conducted under GLP, male and female rats were dosed by gavage with this chemical at 0, 60, 200 and 700 mg/kg/day. At 700 mg/kg some females showed transient reduction in locomotor activity during the early administration period. Bodyweight gain and food consumption at this dose were decreased in both males and females. Blood chemistry revealed increases in cholinesterase activity and total bilirubin levels in males and GPT in females and decreases of chloride levels in males and glucose levels in females. Histopathological examination in males dosed at 700 and 200 mg/kg/day revealed increases of hyaline droplets and eosinophilic bodies in the renal tubules which was accompanied by an increase in relative kidney weight. There was a decrease of splenic weight in females at 700 mg/kg/day, but no histological abnormalities were detected. No changes considered to be attributable to sulfolane were observed on urinary and haematological examinations at any dose. Kidney lesions tended to recover and the other changes related to the chemical disappeared after a 14 day recovery period. The NOAEL was 60 mg/kg/day for male rats and 200 mg/kg/day for female rats.

The chemical was not mutagenic in bacteria [OECD TG 471 and 472] and did not induce chromosome aberrations in mammalian cells in vitro [OECD TG 473] either with or without metabolic activation.

In a reproduction/developmental toxicity screening test [OECD 421]) rats were dosed at 0, 60, 200, or 700 mg/kg/day

by gavage for 41 to 50 days from 14 days prior to mating to day 3 of lactation. Some mortality occured in the high-dose group. There was a decrease in body weight gain and food consumption of males and females during the pre-mating period, at 700 mg/kg. The number of oestrus cycles was decreased in the 700 mg/kg group. Four dams lost all their pups during the lactation period in the 700 mg/kg group. Birth index, live index, number of pups on days 1 and 4 of lactation, viability index and body weights of pups of both sexes on days 0 and 4 of lactation decreased, and the number of still births increased in the 700 mg/kg group. Birth index and the number of pups on day 0 and 4 of lactation decreased in the 200 mg/kg group. The NOAEL for reproductive and developmental toxicity was 60 mg/kg/day. There were no treatment-related findings in the external appearance, general conditions and necropsy findings in offspring.

Environment

The chemical has a log Pow of –0.77, a vapour pressure of 0.0083 hPa at 20°C and a water solubility of greater than 100 g/l. Fugacity model Mackay level III calculations suggest that the chemical will distribute almost completely to water if released to the aquatic compartment and equally to soil and water if released into air or soil separately or simultaneously to all three compartments.. The chemical is not readily biodegradable (10% after 14 days), and is hydrolytically stable (t1/2 greater than 1 year at pH 4, 7 and 9, 25°C). It can be biodegraded after acclimatisation of activated sludge and by a variety of bacterial cultures, and may be substantially biodegradable. Inorganic sulphate has been identified as the final degradation product of sulfolane metabolism. The chemical has been shown to have low potential for bioaccumulation. Indirect photo-oxidation by hydroxy radicals is predicted to occur with a half-life estimated at 9.7 h (calculated using AOPWIN rate constant, 1.328×10^{-11} cm^3/molecule/sec).

In an acute fish toxicity study [OECD TG 203, *Oryzias latipes*] a 96-hLC_{50} > 100 mg/l was reported. In *Daphnia magna* [OECD TG 202], an acute toxicity value of 48h EC_{50} = 852 mg/l was reported. The results in algae [OECD 201] were an E_rC_{50} (72h) >1000 mg/l,E_bC50 = 500mg/ l and a $NOEC_r$ (72 h) = 556 mg/l, $NOEC_b$ = 171 mg/l. The chronic toxicity to *Daphnia magna* [OECD 211] was a NOEC (21d, reproduction) of 25 mg/l and an LC_{50} (21d, parental) > 100 mg/l.

In a study to determine plant toxicity [Environment Canada protocol, lettuce (*Lactuca sativa*), carrot (*Daucus carota*), alfalfa (*Medicago sativa*) and timothy (*Phleum pratense*)] it was determined that plants were generally most sensitive to sulfolane in till and least sensitive in loam. A five day seed germination/root elongation test conducted using lettuce (*Lactuca sativa*) reported NOEC values of 290 mg/kg (root elongation) and 570 mg/kg (seed germination) for lettuce grown in fine-textured soil.

Exposure

Production of the chemical during 2003 was 1100 t/year in Japan. Global production in 2003 was approximately 13,300 t/year. Geographically, production was divided between sites in the Americas (35-45%), Asia (20-30%) and Europe/Africa (35-45%).

The major use of Sulfolane is as a solvent for extraction of aromatic hydrocarbons from oil refinery streams and acid gas purification. These uses account for approximately 80% of production. A number of minor uses (accounting for 20% of production) include fractionation of wood tars, tall oil and other fatty acids, electronic applications, textile manufacturing and finishing, as a plasticizer and as a solvent in pharmaceutical manufacturing. Other uses mentioned in the literature include solvent for jet printing inks, a component of hydraulic fluid, a curing agent for epoxy resins and medicinal application (although this latter application is thought to exist in the patent literature only).

Monitoring studies performed in the vicinity of gas processing facilities in Canada have shown that environmental release of sulfolane during its use in these facilities is possible. Sulfolane was detected in soil, bedrock and shallow till aquifers, wetlands and creeks near these facilities. It was also detected in wetland vegetation.

There is low potential for exposure to workers during production of the chemical. It is manufactured in a closed

system and transferred directly from the reactors into storage tanks. There is potential exposure to workers during drum filling. This operation is performed on 16 days per year for 7 hours each day. The concentration of sulfolane close to the drums has been measured at 0.2 ppm. There is potential exposure to workers at user sites. Since the predominant use of sulfolane is as a solvent in commercial extraction processes there is little potential for direct consumer exposure, however there is a potential for indirect human exposure via drinking water and food crops in areas surrounding processing plants.

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

Human health: The chemical is a candidate for further work. The chemical possesses properties indicating a hazard for human health (reproductive and developmental toxicity). Based on data presented by the Sponsor country worker exposure in sites manufacturing the chemical is controlled. No information is available for occupational exposure in industries using the chemical nor for indirect human exposure via drinking water and food crops in areas surrounding processing plants. It is therefore recommended that member countries perform an exposure assessment for industrial users and indirect human exposure, and if then indicated, risk assessments be performed.

Environment: The chemical is currently of low priority for further work because of its low hazard potential.