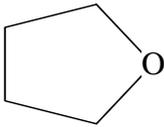


SIDS INITIAL ASSESSMENT PROFILE

CAS No.	109-99-9
Chemical Name	Tetrahydrofuran
Structural Formula	

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR**Human Health**

In short-term tests with fish, daphnids and algae the following results were found: *Pimephales promelas*: 96h-LC50=2160 mg/l; *Daphnia magna*: 24h-LC50=5930 mg/l; *Scenedesmus quadricauda*: NOEC(8 days)=3700 mg/l. A fish early life stage test with the fathead minnow was performed and showed a NOEC of 216 mg/L. With an assessment factor of 50 a PNEC of 4.32 mg/l can be calculated from the fish early life stage test.

THF has low acute toxicity by all routes of exposure. In rats the LC50 (4hr) is 53.9 mg/l (18,271 ppm). It is irritating to the skin, mucous membranes and the eyes. Repeated exposures to THF in laboratory animals has produced mainly transitory narcosis and mild adaptive responses – respiratory and mucous membrane irritation, exacerbation of nephropathy in male rats, adrenal and liver toxicity all at high dose levels (lowest oral NOEL in a 90-day study of 400 mg/kg body weight, and lowest inhalation NOEC in a 90-day study of 200 ppm). In animals, no effects on reproductive performance was observed (two-generation oral study in rats with a NOEL of 300 mg/kg body weight), and signs of developmental toxicity were observed at levels (inhalation NOECs of 500 ppm for maternal effects in rats and 610 ppm for fetal effects in mice) which also produced effects in the maternal animals. The fetal effects observed were intrauterine mortality, early resorptions, and slight reduction in breastbone ossification. No teratogenic effect was seen. All *in vitro* genetic toxicity studies were negative for mutational/chromosomal effects, both with and without metabolic activation. Four *in vivo* genetic toxicity studies in mammals were conducted. Two were negative (an unscheduled DNA synthesis study in rats and a bone marrow chromosomal aberration assay in mice), and two were equivocal (sister chromatid exchange assay in mice and the male response in a mouse micronucleus test, the female response was negative). The weight of evidence indicates that THF is non-genotoxic.

In rodents, THF produced some evidence of carcinogenicity in male rats (renal tubule epithelial adenoma or carcinoma combined) and clear evidence of carcinogenicity in female mice (hepatocellular neoplasms) following inhalation exposures to 600 ppm and 1800 ppm, and to 1800 ppm, respectively. The doses used in both experiments were 0, 200, 600, and 1800 ppm. Studies designed to further understand these findings are underway.

Environment

Tetrahydrofuran (THF) is a liquid at room temperature and boils at 66°C. Fugacity models suggest that THF would

be found in the environmental compartment where it would be released. Estimation of photodegradation by hydroxyl radicals in air is rapid and hydroxyl radical reaction half-life is estimated at 7.3 hours. THF released to the environment could partition to the water compartment, where it is readily biodegradable but would not degrade through hydrolysis. Bioaccumulation of THF is not expected because of its very low octanol/water partition coefficient. Based upon physical and chemical properties, production, use patterns, and environmental monitoring levels in the low ppb range, the environmental exposure potential is expected to be low.

Exposure

Tetrahydrofuran is a chemical used mainly in the production of polytetramethylene ether glycol (PTMEG), a component of synthetic polymers. It is also used as a solvent, an intermediate and in adhesives. Germany has also reported the use of THF as both a stain remover and for use to delete mordant dyes in products available to consumers. Total production for 1999 was 551 million pounds of which 78% were for PTMEG synthesis in closed systems; the remainder was used for intermediates, agriculture, industrial chemicals, pharmaceuticals and solvents. Worker exposure at production and use facilities shows air levels (on average less than 10 ppm) well below any designated exposure limits. Consumer exposure is rare and occurs on a sporadic basis during the use of plastic pipe solvent cements. Plumbers who use these materials also can have exposures. Workplace exposure monitoring is well below current US OSHA and ACGIH standards/guideline, of 200 ppm, 8 hour daily values and short-term value of 250 ppm (15 minutes, STEL). Monitoring of THF exposure of plumbers during use of THF as a solvent cement for plastic pipe did not exceed the above values. However, it may be noted that the substance seems to be an efficient skin penetrant. Release to the environment from PTMEG is no more than 1% of the THF produced or handled. Other environmental exposures during regular use would also be low.

NATURE OF FURTHER WORK RECOMMENDED

Work is currently underway to determine the mechanism of the carcinogenic response in the rat (by measuring alpha- β globulin in kidneys of THF-treated-rat) and mouse (cell proliferation studies in liver of THF-treated mice). There are also experiments planned to assess the metabolic fate of THF in both rats and mice.