Recommendation from Scientific Expert Group

on Occupational Exposure Limits

for Tetrahydrofuran

8 hour TWA : $50 \text{ ppm } (120 \text{ mg/m}^3)$

STEL : $100 \text{ ppm } (300 \text{ mg/m}^3)$

Additional classification : "Skin"

Substance:

Tetrahydrofuran H₂C C₁

 H_2C C_2H H_2C C_2H

Synonyms: Butylene oxide, 1,4-epoxybutane

EINECS N° : 203-726-8

EEC N° : 603-025-00-0 Classification : F; R11-19 Xi; R36/37

CAS N° : 109-99-9

MWt : 72.11

Conversion factor (20°C, 101kPa) : $3.00 \text{ mg/m}^3 = 1 \text{ ppm}$

Occurrence/use:

THF is a colourless, volatile liquid with a MPt of -108.5°C and a BPt of 67°C. It is highly flammable and has an ether-like odour and a pungent taste. The vapour pressure is 17.5kPa at 20°C and the odour threshold is 20-50 ppm (60-150 mg/m³).

THF is produced mainly by catalytic hydrogenation of maleic acid anhydride or furan. It has a production rate in the European Communities in excess of 1000 tonnes per annum. It is used in industry as a solvent for a variety of resins, plastics and elastomers, and as an adhesive for joining plastic parts. Occupational exposure levels are greatest during use as a solvent adhesive, with short term levels of up to 263 ppm (789 mg/m³).

Health Significance:

The SEG discussed the document (SEG/CDO/2) which was co-produced by the Swedish Criteria Group for Occupational Standards and the Dutch Expert Committee for Occupational Standards.

In animals, THF is rapidly absorbed by the lungs and through the skin. It is distributed relatively uniformly in the body, with slightly higher concentrations observed in adipose tissues.

THF has low acute toxicity, reported LC50 values being in the region of 20,000 ppm (60,000 mg/m³). Death is preceded by narcosis.

Inhalation studies in animals indicate that the mucous membranes of the eyes and respiratory tract, and the central nervous system are the critical target tissues. Liver and kidney damage have also been noted. Although there are no controlled human studies, comparable effects have been observed in reports on workers exposed to THF vapour.

Concentration-related effects on nasal and tracheal ciliary beating have been reported, with minimal, transient, effects at 100 and 250 ppm (300 and 750 mg/m³) (Ikeoka et al, 1984; Ohashi et al, 1983). Exposure of rats to 200 ppm (600 mg/m³) for 3 hours also caused slight irritation of the nose and eyes (Katahira et al, 1982a). CNS effects have been observed following exposure of rats to 3000 ppm (9000 mg/m³) 3 h/day, 5 days/week for 8 weeks (Kawata et al, 1986). Increases in serum enzymes, indicative of liver damage, have been observed in rats exposed to THF at 1000 ppm (3000 mg/m³) 4h/day, 5 days/week for 12 weeks (Katahira et al, 1982b). Similar indications have been seen in workers exposed to THF vapour at less than 1000 ppm (3000 mg/m³) (Horiushi et al, 1967). A 13-week inhalation study, conducted by Chhabra et al (1990), identified NOAELs for systemic effects (CNS and liver damage), of 1800 ppm (5400 mg/m³) in rats and 600 ppm (1800 mg/m³) in mice.

Thus, 100 ppm (300 mg/m³) may be considered as the minimal effect level.

THF may lower the threshold for epileptic seizures.

Recommendation:

Studies showing reduction in ciliary beating (Ikeoka et al, 1984; Ohashi et al, 1983) and irritation of the nose and eyes of the rat (Katahari et al, 1982a) established a lowest observed effect level of 100 ppm (300 mg/m³) and were considered to be the best available basis for setting exposure limits. An uncertainty factor of 2 was considered to be appropriate in view of the transient nature of the minimal effects observed. The recommended 8-hour TWA is 50 ppm (150 mg/m³). To prevent short term exposure to irritant levels an STEL (15 mins) of 100 ppm (300 mg/m³) is recommended.

Skin penetration may make a substantial contribution to the total body burden so a skin notation is also required.

Additional information on human health effects should be obtained.

At the levels recommended, no measurement difficulties are foreseen.

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