Recommendation of the Scientific Committee on Occupational Exposure Limits for 1-Methoxypropan-2-ol

8 hour TWA	:	100 ppm (375 mg/m³)
STEL (15 mins)	:	150 ppm (563 mg/m³)
Additional classification	:	"skin"

Substance:

1-Methoxypropan-2-ol $H_3C\text{-}O\text{-}CH_2\text{-}CHOH\text{-}CH_3$

Synonyms	:	Propyleneglycol-1-mono-methylether; PGME	
EINECS N°	:	203-539-1	
EEC N°	:	603-064-00-3	Classification: R10
CAS N°	:	107-98-2	
MWt	:	90.12	
Conversion factor (20°C, 101kPa)	:	3.75 mg/m³ = 1 ppm	

Occurrence/use:

1-Methoxypropan-2-ol is a colourless liquid with a sweet, ether-like odour. It is soluble in water and a number of organic solvents. It has a BPt of 120°C and a vapour pressure of 1.2 kPa at 20°C. It has a vapour density of 1.3 times that of air.

1-Methoxypropan-2-ol is used industrially as a solvent for paints, lacquers, resins, oils and fats. The production rate in the EEC is in excess of 1000 tonnes per annum.

Commercial methoxypropanol contains both 1-methoxypropan-2-ol (alpha isomer 95-99%) and 2-methoxypropan-1-ol (beta isomer, 1-5%). For most of the studies mentioned in this summary, the exact composition of the test substance is not known.

Health Significance:

1-Methoxypropan-2-ol is well-absorbed orally, by inhalation and percutaneously (Rowe et al, 1954).

Volunteers exposed to 95 ppm (356 mg/m³) 1-methoxypropan-2-ol found the odour intolerable at first but became acclimatised within 25 mins (Stewart et al, 1970). Mild eye irritation was reported by 2 out of 6 individuals after 1-2h exposure at this level. Exposure to 231-249 ppm (866-934 mg/m³) for 45-60 mins produced irritation of the eyes, nose and throat. Signs of CNS depression were recorded at 1000 ppm (3750 mg/m³). In a more recent study, Emmen et al (1997) investigated the eye irritation potential of 1-methoxypropan-2-ol in 12 volunteers, who were exposed to 1-methoxypropan-2-ol at concentrations of 100 or 150 ppm (375 or 563 mg/m³) for 2.5 hours. A masking agent (diethyl ether) was used to minimise responses to the odour. No effects were reported at 100 ppm (375 mg/m³). Minimal subjective effects were reported at 150 ppm (563 mg/m³), but because there were no detectable changes in objective measures of eye irritation, this concentration is considered to be a NOAEL. The difference in results between these two studies is likely to be due to the awareness of the odour resulting in reporting of subjective symptoms in the earlier study.

The acute toxicity of 1-methoxypropan-2-ol to experimental animals is low. Direct application of the liquid results in slight skin and eye irritation (Rowe et al, 1954).

Repeated exposure of rats and mice to 300 and 1000 ppm (1125 and 3750 mg/m³) 1-methoxypropan-2-ol, 6h/d, 5d/w for 2 weeks resulted in slight transient narcotic effects, whereas at 3000 ppm (11,250 mg/m³) some signs of kidney and liver lesions and depressions of the CNS were noted (Miller et al, 1981). Histopathological effects were not seen in either rats or mice. Following exposure of rabbits to 300, 1000 and 3000 ppm (1125, 3750 and 11,250 mg/m³), 6h/d, 5d/w for 13 weeks, slight changes in the liver were seen at the highest exposure level only (Landry et al, 1983).

1-Methoxypropan-2-ol was not genotoxic in a limited range of in vitro tests. No carcinogenicity data are available.

Initial studies on the developmental toxicity of 1-methoxypropan-2-ol were done with mouse, rat and rabbit using oral administration or subcutaneous injection (Stenger et al, 1972). The dosages were — depending on the route of application — up to 1800 mg/kg/day in mice (day 1 to 18 of gestation), up to 740 mg/kg/day in rats (day 1 to 21 of gestation), and up to 924 mg/kg/day in rabbits (day 6 to 18 of gestation). There was no evidence of embryotoxicity, teratogenicity, fetotoxicity or maternal toxicity at the doses tested. Only rat fetuses showed delayed ossification of the skull at the highest dose level of 740 mg/kg/day.

Rats (20 animals per group) were exposed to 0, 200 and 600 ppm (0, 750 and 2250 mg/m³) for 6 hours per day from day 6 to day 17 of gestation (Doe et al, 1983). The litters were observed until the third day postpartum and the number of surviving pups and their weight development were registered. The proportion of live pups on day 1 postpartum, the proportion of pups surviving day 3 and the mean live pup weights were similar to controls. Toxic effects on dams were not observed.

Well-documented descriptions of prenatal toxicity studies have been published on rats exposed from day 6 to day 15 of gestation and rabbits exposed from day 6 to day 18 of gestation. Concentrations of 1-methoxypropan-2-ol used were 0, 500, 1000 and 3000 ppm (0, 1875, 3750 and 11,250 mg/m³) for 6 hours daily, where 3000 ppm approximately corresponds to the vapour saturation (Hanley et al, 1984). 31 to 33 animals per experimental group were tested from both animal species. In rats, there was no evidence for embryotoxic or teratogenic effects up to the highest concentration tested. Slight fetotoxicity (delayed ossification of the sternum) was observed in some fetuses at 3000 ppm (11,250 mg/m³), a concentration that also caused clinical symptoms of CNS depression in the dams. Neither maternal nor embryonic, teratogenic or fetal effects were observed in the rabbits.

In a 2-generation study (Morrisey et al, 1989), male and female CD1 mice received 1-methoxypropan-2-ol in drinking water at concentrations of 0, 0.5, 1.0 and 2% (approximately 0.95, 1.89 and 3.33 g/kg/day). No change in reproduction parameters and no impairment of fertility were observed in the adult animals until the second generation, in which a reduction in epididymal and prostate weight was detected in the highest dosage group.

Recommendation:

The study of Emmen et al (1997), establishing a NOAEL of 150 ppm (563 mg/m³) for eye irritation in human volunteers with 2.5 hours exposure, was considered to be the best available basis for proposing occupational exposure limits for 1-methoxypropan-2-ol. In order to protect against exposure to concentrations that could result in irritation, the SCOEL recommended an 8-hour TWA of 100 ppm (375 mg/m³) and a STEL (15 mins) of 150 ppm (563 mg/m³). In reproductive toxicity studies, there were no embryotoxic, teratogenic or fetotoxic effects at concentrations up to 1500 ppm (5625 mg/m³) in rats and up to 3000 ppm (11,250 mg/m³) in rabbits. Thus the NOAEL for developmental toxicity is greater than the proposed 8-hour TWA by a factor of at least 15. Studies with oral application of relatively high doses support the minor reproductive toxicity potential of the substance.

A “skin” notation was recommended as dermal absorption could contribute substantially to the total body burden.

At the levels recommended, no measurement difficulties are foreseen.

Key Bibliography:

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