



Recommendation from the Scientific Committee on Occupational Exposure Limits for Aerosols of 2-(2-Methoxyethoxy)ethanol

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Table of Contents

Health Significance	4
Conclusion	5
References.....	7



Recommendation from the Scientific Committee on Occupational Exposure Limits for for 2-(2-Methoxyethoxy)ethanol*

8 hour TWA:	10 ppm (50.1 mg/m ³)
STEL:	-
Additional classification:	skin

Substance

Name	2-(2-Methoxyethoxy)ethanol [111-77-3]	
Synonyms	DEGME, diethylene glycol methyl ether, methyl diglycol ether	
EINECS No	203-906-6	
CAS No	111-77-3	
Mwt:	120.2	
Conversion factor (20°C, 101 kPa):	5.01 mg/m ³ = 1 ppm	

2-(2-Methoxyethoxy)ethanol (DEGME) is a liquid. It is miscible with water (log Pow = -0.682). Mpt is -65°C, bpt 190-196°C, vapour pressure 0.24 hPa.

It is used as a fuel additive, a chemical intermediate in synthesis, a solvent in paints, lacquers and varnishes, a cleaning and washing agent, and as a disinfectant (Risk Assessment Report, EN 1998).

* This SCOEL Summary Document is based on Risk Assessment Report 2-(2-Methoxyethoxy)ethanol, Final report 1, September 1998, EUR 18999 EN.



Health Significance

Dermal absorption through human skin in vitro was 0.206 ± 0.156 mg/cm²/h (Dugard et al. 1984). No studies on absorption, metabolism and excretion in animals or humans are available. Rats metabolized the structurally-similar diethylene glycol dimethyl ether, when given orally, to 2-(methoxyethoxy) acetic acid and methoxyacetic acid (70% and 6%, respectively). DEGME itself was a minor product (max. 0.3%) (Cheever et al. 1988). This study indicates that DEGME will be metabolised, probably like other aliphatic alcohols, to its corresponding acid — in this case to 2-(methoxyethoxy) acetic acid and, after cleavage of the ether bond, also to methoxyacetic acid. It is known that alkoxyacetic acids are eliminated slowly (ECETOC 1995). The half-life of 2-ethoxyacetic acid after oral application is 6 times shorter in rats than in humans (Groeseneken et al. 1988). Therefore, it may be assumed that the acid metabolites of DEGME also have a long half-life which might be even longer in humans than animals.

Acute toxicity is low with oral LD₅₀ in mouse, rat, guinea pig and rabbit from 4000 to 9000 mg/kg bw. Inhalation toxicity is low. Lethality in rats was not observed after up to 8 h exposure to a saturated atmosphere at 20°C (concentration not stated) (BASF AG 1960; Union Carbide 1984). Dermal toxicity is in the range of oral toxicity with LD₅₀ 6540-20400 mg/kg bw in rabbits (Union Carbide 1967, 1984). Target organs are liver, kidney and the central nervous system (narcosis).

Irritation on skin and eye of the rabbit is low (Union Carbide 1984).

DEGME is not sensitising in the guinea pig maximisation test (Bury 1997) or in a human maximisation test as 25% solution (Kligman, 1972).

In a 6-week oral study in rats with doses of 900, 1800 and 3600 mg/kg bw the NOEL was 900 mg/kg bw. At 1800 mg/kg bw decreased body weight gain and food consumption were observed. At 3600 mg/kg bw the absolute and relative testis weight was decreased. 50% of the rats had testis atrophy with degenerated spermatozoa in the epididymus and hypospermia. 90% had proteinaceous casts in the urine. No histopathological effects on the liver were noticed (Krasavage and Vlaovic 1982).

In a 90-day OECD guideline-like study 10 Fischer 344 rats per sex were whole-body exposed 6 h/d, 5 d/week to DEGME vapour in concentrations of 150, 490 and 1060 mg/m³. The highest exposure level was the maximum practical attainable. The NOEL was ≥ 1060 mg/m³ (Miller et al. 1985). Assuming a 6 h inhalation volume of 0.06 m³ for a rat of 250 g bw and the absorption to be 100%, the corresponding dose is 240 mg/kg bw in the highest dose group.

In a 13 week study, groups of 6 male Hartley guinea pigs (control 7 animals) were dermally exposed to 40, 200 or 1000 mg DEGME/kg bw (neat, occlusive) for 6 h/d, 5 d/week. The treatment was not irritating to the skin of the animals. A dose-related increase in serum LDH was observed from 200 mg/kg bw, significant at 1000 mg/kg bw. Spleen weight was decreased from 200 mg/kg bw. In all dosed groups urinary calcium level was increased without renal mineralization or damage. Incidences of mild periportal hepatocellular fatty changes were increased in all dosed groups (0/7, 2/6 [not significant], 6/6, 6/6). The severity of the changes did not, however, increase with dose. Focal coagulation necrosis of the liver was observed in all groups including controls and was not dose-related. Organ weights were not altered. Testes changes were not seen histopathologically (Hobson et al. 1986). Historical incidences of fatty changes in the liver of guinea pigs are not available. The dose-response relationship in this study is rather flat considering that a 25-fold increase in dose from 40 to 1000 mg/kg bw did not lead to an increase of the severity of the



hepatic fatty changes. It is unclear whether the focal necrosis observed in all animals including controls is related to the hepatic findings. Moreover, the weight of the liver was not increased. The biological significance of these findings is unclear.

22 rats per group were gavaged with 200, 600 or 1800 mg DEGME/kg bw daily at days 7 to 17 of gestation. 600 mg/kg bw was the NOEL for maternal toxicity. At this dose the number of pups surviving 4 days was decreased, 2.4% of the fetuses had visceral malformations, 25.4% had unilateral or bilateral thymic remnants and the degree of ossification was delayed. At 1800 mg/kg bw maternal body weight gain, food consumption and thymus weight were decreased. The duration of gestation was increased 2 days. The number of pups surviving 4 days was decreased, the incidence of external malformations was increased, 28% of the fetuses had visceral malformations, 100% had unilateral or bilateral thymic remnants, 52.8% had dilated renal pelvis and the degree of ossification was delayed. The NOEL for fetotoxicity was 200 mg/kg bw (Yamano et al. 1993).

DEGME was gavaged to rats in doses of 720 or 2165 mg/kg bw on gestational days 7 to 16. 720 mg/kg bw was the NOEL for maternal effects. From 720 mg/kg bw the incidences of delayed cranial and appendicular skeleton ossification as well as of dilated renal pelvis were increased. At 2165 mg/kg bw fetal weight and litter size were reduced and 2 of 23 litters were completely resorbed. Malformations especially of the cardiovascular system were significantly increased. Maternal effects consisted of slightly reduced body weight gain and food consumption. The NOEL for fetotoxicity was < 720 mg/kg bw (Hardin et al. 1986).

Rabbits were given daily dermal application of 50, 250 or 750 mg/kg on gestational days 6 to 18. 50 mg/kg bw caused no fetal effects. 250 mg/kg was the NOEL for maternal effects. From this dose the incidences of delayed ossification of the hyoid and sternbrae and cervical spur were increased. At 750 mg/kg bw. increased incidences of resorptions, mild forelimb flexure, dilation of the renal pelvis, retrocaval urether and delayed ossification of the skull were seen (Scortichini et al. 1986).

DEGME was not mutagenic in 2 tests with *S. typhimurium* (ICI PLC 1980; BASF 1989) and did not induce chromosomal aberrations in V79 cells in vitro (Müller 1997).

No data on carcinogenicity are available.

Conclusion

Since the minimal hepatic effects in guinea pigs did not occur in the rat at doses which were 6 to at least 20-fold higher, this study is not used for deriving an OEL. The 90-day inhalation study in rats, resulted in a NOEL of 1060 mg/m³ which corresponds to about 240 mg/kg bw. The developmental study in rats with gavage application resulted in a NOEL for fetotoxicity of 200 mg/kg bw. In the developmental study with rabbits and dermal application a NOEL of 50 mg/kg bw. was obtained. Assuming a similar (100%) absorption after oral, inhalative and dermal exposure and an 8 h inhalation volume of 10 m³ at the workplace, 50 mg/kg bw correspond to 350 mg/m³ (70 ml/m³). For interspecies extrapolation regarding systemic effects it should be noted that the metabolites of DEGME presumably have a longer half-life in humans than in animals. As shown for 2-ethoxyacetic acid the half-life is 6 times longer in humans than in rats. As a worst-case approach it is assumed that the effects of DEGME are governed by the time-concentration product. The dose per kg bw for workers should therefore be accordingly lower than the NOEL of 50 mg/kg bw obtained in the animal experiment. Considering the difference in the DEGME metabolite between animals and man a factor of 5 is applied



resulting in an OEL of 10 ppm. A skin notation is warranted because reproductive toxicity was observed after dermal application. No sensitizer designation is necessary.



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