

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: 2-Methoxyethanol File (CAS # 109-86-4)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

SUBJECT: Screening Level for 2-methoxyethanol (CAS # 109-86-4)

DATE: July 17, 2015

The initial threshold screening level for 2-methoxyethanol (CAS # 109-86-4) is 20 $\mu\text{g}/\text{m}^3$ with an annual averaging time. The ITSL was established in 1990 and was based on the impending EPA (1991) RfC based on the subchronic rabbit and rat inhalation study by Miller et al. (1983), which showed testicular effects. The averaging time for the ITSL was originally set at the default of 24 hours, but is now being set at annual as supported by the key study and critical effect.

2-Methoxyethanol (CAS # 109-86-4) also known as methyl cellosolve and ethylene glycol monomethyl ether, is a clear, colorless, flammable liquid with a mild ether-like odor and has a molecular weight of 76.09 g/mol. 2-Methoxyethanol is a member of the glycol ether group of compounds, which are known for the ability to dissolve a variety of different types of chemical compounds and for the ability to dissolve in water and other solvents. It is used mainly as a solvent for varnishes, dyes, resins, and as an additive in airplane deicing solutions.

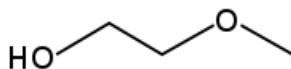


Figure 1. Structure of 2-methoxyethanol.

EPA's RfC was used to derive the ITSL. EPA's RfC used the Miller et al. (1983) study where, "groups of New Zealand white rabbits (5/sex/dose) and Sprague-Dawley rats (10/sex/dose) were exposed to 0, 30, 100, or 300 ppm ethylene glycol monomethyl ether (0, 93, 311, or 934 mg/m^3 , assuming 25°C and 760 mmHg) 6 hours/day, 5 days/week for 13 weeks. The duration-adjusted exposure concentrations were 0, 17, 56, and 167 mg/m^3 , respectively. Toxicity was assessed by clinical observations, body and organ weights, hematology, clinical chemistry, urinalysis (rats only), and gross and histopathological examination of major organs including respiratory tract (including lungs, nasal turbinates, and trachea), heart, liver, kidney, bone marrow, testes, uterus, and ovaries" (EPA, 1991).

"In the rabbits, 2/5 females exposed to 100 and 300 ppm and 2/5 males exposed to 300 ppm died during the course of the study. The deaths, however, could not be conclusively attributed to ethylene glycol monomethyl ether exposure. Effects reported in both sexes of rabbits exposed to 300 ppm included reduced body weight, hematological changes (pancytopenia), lymphoid tissue atrophy (thymus) and a significant decrease in testicular weight with small flaccid testes in the males. A slight to moderate decrease in testes size was also reported in 2/5 and 4/5 male

rabbits exposed to 30 and 100 ppm, respectively. Microscopic lesions included degenerative changes in the germinal epithelium of the testes in 3/3, 3/5, and 1/5 male rabbits exposed to 300, 100, and 30 ppm, respectively. The decrease in testes weight was considered to be concentration dependent in the male rabbits. No effects on the reproductive organs of the female rabbits were found. Thymus weights were significantly decreased in both sexes exposed to 300 ppm ethylene glycol monomethyl ether. Based upon the testicular effects in rabbits a NOAEL of 30 ppm (HEC = 17 mg/m³) and a LOAEL of 100 ppm (HEC = 56 mg/m³) is identified” (EPA, 1991).

“No rats died over the course of the experiment. The authors reported a significant decrease in body weight in the male rats exposed to 300 ppm and in the females exposed to 100 ppm or more. Effects reported in both sexes of rats exposed to 300 ppm included hematological changes (pancytopenia), lymphoid tissue atrophy, a decrease in liver weight, and changes in clinical chemistry parameters. In the 300 ppm group (male and female rats) the mean values for total serum protein, albumin and globulins were lower than the control values. A significant decrease in testicular weight and small flaccid testes were also reported in the male rats exposed to 300 ppm. Microscopic examination showed moderate to severe degeneration of the germinal epithelium in the seminiferous tubules at the highest exposure. There were no microscopic changes in the testes in the animals exposed to 100 or 300 ppm ethylene glycol monomethyl ether. The authors found no effects in the reproductive organs of the female rats. In rats, the LOAEL for degenerative effects on the testes is 300 ppm (HEC = 167 mg/m³), and the NOAEL is 100 ppm (HEC = 56 mg/m³)” (EPA, 1991).

EPA’s RfC derivation used the critical effect of testicular effects from Miller et al., (1983). The NOAEL of 93 mg/m³ was used in the derivation of the RfC. Conversion factors were determined by using the molecular weight of 2-methoxyethanol of 76.09 g/mol, assuming 25°C and 760 mmHg.

$$NOAEL \left(\frac{mg}{m^3} \right) = \frac{30 \text{ ppm} \times 76.09}{24.45} = 93 \text{ mg}/m^3$$

$$NOAEL_{ADJ} = 93 \text{ mg}/m^3 \times \frac{6 \text{ hours}}{24 \text{ hours}} \times \frac{5 \text{ days}}{7 \text{ days}} = 17 \text{ mg}/m^3$$

“The NOAEL_{HEC} was calculated for a gas:extrarrespiratory effect assuming periodicity was attained. Since the blood:air partition coefficient values (b:a lambda) are unknown for rats (a) and humans (h), a default value of 1 is used for this ratio” (EPA, 1991).

$$NOAEL_{HEC} = NOAEL_{ADJ} \times \frac{b: a \text{ lambda} (a)}{b: a \text{ lambda} (h)} = 17 \text{ mg}/m^3 \times \frac{1}{1} = 17 \text{ mg}/m^3$$

An uncertainty factor of 1000 was used: 10 for protection of sensitive humans; 10 for extrapolation from subchronic to chronic; and 10 was used to account for both interspecies extrapolation (because a dosimetric adjustment is used) and for database deficiencies (e.g., minimal evaluation of respiratory effects). This gives an RfC of 2E-2 mg/m³.

Rule 232(1)(a) states that a RfC can be used as an ITSL, therefore the ITSL for 2-methoxyethanol is 20 µg/m³. Rule 232(2)(b) states that the default averaging time is 24-hours; however, in this case the critical effect and study duration support an annual averaging time as allowed under Rule 229(2)(b).

References:

Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality.

EPA. 1991. Integrated Risk Information System. 2-Methoxyethanol (CASRN 109-86-4). Retrieved data on 5/14/2015. Available online at: <http://www.epa.gov/iris/subst/0525.htm>

Miller RR, Ayres JA, Young JT, and McKenna MJ. 1983. Ethylene glycol monomethyl ether. I. Subchronic vapor inhalation study with rats and rabbits. *Fund. Appl. Toxicol.* 3(1):49-54.

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