

2-Methoxyethanol; CASRN 109-86-4

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

STATUS OF DATA FOR 2-Methoxyethanol

File First On-Line 05/01/1991

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	yes	05/01/1991
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — 2-Methoxyethanol

CASRN — 109-86-4

Not available at this time.

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — 2-Methoxyethanol

CASRN — 109-86-4

Last Revised — 05/01/1991

I.B.1. Inhalation RfC Summary

Critical Effect	Exposures*	UF	MF	RfC
Testicular effects	NOAEL: 93 mg/cu.m (30 ppm) NOAEL(ADJ): 17 mg/cu.m	1000	1	2E-2 mg/cu.m
Subchronic Inhalation Studies in Male New Zealand White Rabbits and Sprague-Dawley Rats	NOAEL(HEC): 17 mg/cu.m LOAEL: 311 mg/cu.m (100 ppm) LOAEL(ADJ): 56 mg/cu.m LOAEL(HEC): 56 mg/cu.m			
Miller et al., 1983				

*Conversion Factors: MW = 76.09. Assuming 25C and 760 mm Hg, NOAEL(mg/cu.m) = 30 ppm x 76.09/24.45 = 93 mg/cu.m. NOAEL(ADJ) = 93 mg/cu.m x 6 hours/24 hours, 5 days/7 days = 17 mg/cu.m. 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. NOAEL(HEC) = NOAEL(ADJ) x b:a lambda (a)/b:a lambda (h) = 17 mg/cu.m.

I.B.2. Principal and Supporting Studies (Inhalation RfC)

Miller, R.R., J.A. Ayres, J.T. Young and M.J. McKenna. 1983. Ethylene glycol monomethyl ether. I. Subchronic vapor inhalation study with rats and rabbits. *Fund. Appl. Toxicol.* 3(1): 49-54.

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/cu.m, assuming 25C and 760 mm Hg) 6 hours/day, 5 days/week for 13 weeks. The duration-adjusted exposure concentrations were 0, 17, 56 and 167 mg/cu.m, 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.

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/cu.m) and a LOAEL of 100 ppm (HEC=56 mg/cu.m) is identified.

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 30 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/cu.m), and the NOAEL is 100 ppm (HEC=56 mg/cu.m).

In an earlier study by Miller et al. (1982) groups of 10 male New Zealand white rabbits were exposed to 0, 3, 10 or 30 ppm ethylene glycol monomethyl ether (0, 9, 31 or 93 mg/cu.m, assuming 25C and 760 mm Hg) 6 hours/day, 5 days/week for 13 weeks. The authors did not report any treatment-related effects on general appearance, body weight, testes weight, or gross and histological examination of the major organs and testes. These two studies (Miller et al., 1982, 1983) indicate that rabbits are more sensitive to the effects of ethylene glycol monomethyl ether than rats due to the increased mortality and persistence of testicular effects at higher exposures and that the threshold level for testicular effects in rabbits is >30 ppm. In rabbits, the NOAEL is 30 ppm (HEC=17 mg/cu.m).

I.B.3. Uncertainty and Modifying Factors (Inhalation RfC)

UF — An uncertainty factor of 10 each is used to account for protection of sensitive humans and for extrapolation from subchronic to chronic duration. Another factor of 10 is used to account for both interspecies extrapolation (because a dosimetric adjustment is used) and for database deficiencies for (e.g., minimal evaluation of respiratory effects).

MF — None

I.B.4. Additional Studies/Comments (Inhalation RfC)

Human case studies report that the neurological and hematological systems are target organ systems for ethylene glycol monomethyl ether toxicity. Data in animals indicate that the testes and the developing fetus are also targets of ethylene glycol monomethyl ether toxicity. Only one human case study examined the possible effects of exposure on the fertility of workers and found no reproductive effects. The rabbit is more sensitive to the testicular effects of ethylene glycol monomethyl ether as compared with rats and mice. The NOAEL(HEC) of 17 mg/cu.m for testicular effects in the rabbit (Miller et al., 1982, 1983) is less than the NOAEL for developmental effects (HEC=31 mg/cu.m) in the rabbit (Hanley et al., 1984). The NOAEL(HEC) for testicular effects in rats is identified as 56 mg/cu.m by both Miller et al. (1983) and Rao et al. (1983).

Case studies in humans report that the neurological and hematological systems are target organ systems of ethylene glycol monomethyl ether toxicity (Cohen, 1984; Cook et al., 1982; Donley, 1936; Greenburg et al., 1938; Parsons and Parsons, 1938; Zavan, 1963). One study examined the possible effects of exposure on the fertility of exposed workers (Cook et al., 1982). Cook et al. (1982) examined the effects of occupational exposure on hematological (anemia, leukopenia) and reproductive parameters (hormone levels, sperm counts, the number of abnormal sperm and the size of testes) were examined in workers in the manufacturing industry. The workers in the production area were exposed to an 8-hour time-weighted average (TWA) concentration of 0.42 ppm or less (1.3 mg/cu.m), while those in the packing and distribution area were exposed to 2-hour TWA concentrations of 5.4-8.5 ppm (16.8-26.5 mg/cu.m) and area atmospheric levels between 4 and 20 ppm (12 and 62 mg/cu.m). There was no significant difference in hematological parameters, hormone levels or sperm effects. A possible decrease in testicular size was the only reproductive effect found in the exposed workers compared to the unexposed controls. The investigators indicated that this decrease in size may have been the result of observer bias because one of three physicians that examined the workers consistently measured lower values and examined more exposed than unexposed workers. This study did not examine neurological endpoints. Both the exposed and unexposed workers were exposed to various other

chemicals in addition to ethylene glycol monomethyl ether. Therefore, a causative relationship between any adverse effect and ethylene glycol monomethyl ether exposure cannot be drawn.

Cohen (1984) reported reversible neurological symptoms (apathy, fatigue, decreased appetite) and asymptomatic hematological effects (macrocytic anemia) in one worker in the manufacturing industry following skin and inhalation exposure to an average concentration of 35 ppm (109 mg/cu.m) ethylene glycol monomethyl ether for 1-1.5 years. The worker was also exposed to methyl ethyl ketone (1-5 ppm) and propylene glycol monomethyl ether (4.2-12.8 ppm). Methyl ethyl ketone may be a neurobehavioral toxicant in humans at higher concentrations.

The older literature (Donley, 1936; Greenburg et al., 1938; Parsons and Parsons, 1938) reported case studies of workers exposed to ethylene glycol monomethyl ether in a plant that produced shirts with a "fused" collar (solvent-treated collar that becomes stiff without the use of starch). The workers were exposed to a solvent containing ethylene glycol monomethyl ether (<3%), isopropanol (74%) and dimethyl phthalate (<3%) for 6 months (Donley, 1936) or to a solvent containing 33% ethylene glycol monomethyl ether and 67% denatured ethanol for up to 112 weeks (Greenburg et al., 1938; Parsons and Parsons, 1938). The workers showed neurological symptoms (encephalopathy, dizziness, fainting, headache, weakness, ataxia, psychopathic disturbances and personality changes) and hematological symptoms (anemia, granulopenia) as well as irritation of the respiratory tract. The workers were exposed to concentrations of ethylene glycol monomethyl ether ranging from 25-76 ppm (78- 237 mg/cu.m), although the exposure levels were probably higher because of improved ventilation conditions implemented before measurement (Greenburg et al., 1938). Zavon (1963) observed similar neurological and hematological effects in workers exposed for up to 7 months to 61-3960 ppm (190-12,324 mg/cu.m) ethylene glycol monomethyl ether used as a printing solvent. The workers recovered when improved plant hygiene reduced the concentration of ethylene glycol monomethyl ether to about 20 ppm (62 mg/cu.m).

In a fertility test, Rao et al. (1983) exposed male and female Sprague- Dawley rats to 0 (30/sex), 30 (30/sex), 100 (20/sex) or 300 (20/sex) ppm ethylene glycol monomethyl ether (0, 93, 311 or 934 mg/cu.m, assuming 25C and 760 mm Hg) 6 hours/day, 5 days/week for 13 weeks. The duration-adjusted exposure concentrations were 0, 17, 56 and 167 mg/cu.m, respectively. The animals were then bred with nonexposed partners. The recovery of fertility was assessed by mating males exposed to 0 or 300 ppm during the post exposure period. Female animals showed no reproductive effects were observed in any exposure group. Male fertility, however, was suppressed in the animals exposed to 300 ppm; only 4/20 of unexposed females were impregnated by the exposed males (HEC = 167 mg/cu.m). The authors observed complete resorptions of all conceptuses in the four successfully impregnated dams. After 13 weeks post exposure, 55% of the exposed males in this group were fertile. Body weights were reduced (8-

13% decrease in terminal body weight) in both sexes of rats exposed to 300 ppm and decreased testicular size and atrophic seminiferous tubules in the males were reported. Fertility was not impaired in the males exposed to 30 or 100 ppm. The NOAEL is 100 ppm (HEC=56 mg/cu.m).

Several investigators have examined the effects of ethylene glycol monomethyl ether on the developing fetus in rabbits, rats and mice (Nelson et al., 1984a,b; Hanley et al., 1984; Doe et al., 1983; Rao et al., 1983). Hanley et al. (1984) exposed groups of 30-31 female Fischer 344 rats and 29-30 female New Zealand white rabbits to 0, 3, 10 or 50 ppm ethylene glycol monomethyl ether (0, 9, 31 or 156 mg/cu.m, assuming 25C and 760 mm Hg) 6 hours/day on gestation days 6-15 (rats) or 6-18 (rabbits). Hanley et al. (1984) also exposed groups of 30-32 female CF-1 mice to 0, 10 or 50 ppm 2- methoxyethanol (0, 31 or 156 mg/cu.m) 6 hours/day during gestation days 6-15. Maternal effects in all species included a transient weight loss in the animals exposed to 50 ppm. The authors observed hematological alterations (decreased hemoglobin levels and packed cell volume) in the exposed rat dams. Developmental effects in the offspring of both rats and mice (increased incidence of minor skeletal variations) were reported in animals exposed to 50 ppm (HEC=156 mg/cu.m). The offspring of rats and mice exposed to 10 ppm or lower (HEC=31 mg/cu.m) had no significant developmental effects. In the rabbits, the authors found developmental toxicity in the offspring of animals exposed to 50 ppm. Effects included an increase in the incidences of malformations, minor skeletal variations and resorptions as well as a significant decrease in fetal body weight. The offspring of the 10 ppm group (HEC=31 mg/cu.m) showed an increased incidence of delayed ossification and a dose-related decrease in fetal body weight. The percentage of implantations resorbed and litters with resorptions significantly increased in the 10 ppm group of rabbits (23/210 and 14/24, respectively), but the authors indicated this difference resulted from unusually low concurrent control values (7/180 and 5/23), and was not treatment-related.

Doe et al. (1983) observed developmental toxicity in the offspring of Wistar rats (20/group) exposed to 0, 100 or 300 ppm ethylene glycol monomethyl ether (0, 311 or 934 mg/cu.m, assuming 25C and 760 mm Hg) 6 hours/day during gestation days 6-17. Maternal body weight gain was reduced in both groups of treated animals. The group exposed to 300 ppm did not deliver any litters, and only 9/20 dams in the 100 ppm group delivered litters (HEC=78 mg/cu.m). The offspring showed reduced numbers, weight and viability (external malformations were not observed). Doe et al. (1983) did not conduct gross and histological examination of the offspring.

Nelson et al. (1984a) reported developmental toxicity in the offspring of Sprague-Dawley rats (8-34/group) exposed to 0, 50, 100 or 200 ppm ethylene glycol monomethyl ether (0, 156, 311 or 622 mg/cu.m, assuming 25C and 760 mm Hg) 7 hours/day during gestation days 7-15. The dams were sacrificed on day 20 of gestation and the fetuses were examined. The authors found total resorption of the fetuses in the animals exposed to 200 ppm. About half of the litters were totally

resorbed in the 100 ppm group while all litters had some resorptions. In the 50 ppm group the authors found a 3-fold increase in resorptions, compared to controls. The offspring from all exposure groups (HEC=156 mg/cu.m) had reduced fetal weights, skeletal defects (rib and tail malformations) and cardiovascular defects (heart abnormalities) (Nelson et al., 1984a).

Nelson et al. (1984b) observed neurological effects in the offspring of male rats exposed to ethylene glycol monomethyl ether for 6 weeks prior to mating and in pregnant female rats exposed during gestation days 7-13. The authors exposed 18 Sprague-Dawley male rats to 25 ppm ethylene glycol monomethyl ether (78 mg/cu.m, assuming 25C and 760 mm Hg) 7 hours/day, 7 days/week for 6 weeks prior to mating with unexposed females (there were no concurrent untreated controls). The brains of 21-day-old offspring had neurochemical changes especially in the brainstem and cerebrum (e.g., dopamine, norepinephrine). They showed no behavioral effects (neuromotor function, activity, simple learning ability). The offspring of pregnant females in both groups similarly exposed to 0 or 25 ppm during gestation days 7-13 or 14-20 (15 animals/group) had similar neurochemical changes. There was a significant difference in avoidance conditioning in the offspring of the group exposed during gestation days 7-13. The concentration of 25 ppm is a LOAEL for developmental toxicity (HEC=78 mg/cu.m) (Nelson et al., 1984b).

Werner et al. (1943a) reported hematological effects of ethylene glycol monomethyl ether in dogs and rats. These authors exposed groups of two dogs (strain not reported) to 0 or 750 ppm (2334 mg/cu.m, assuming 25C and 760 mm Hg) 7 hours/day, 5 days/week for 12 weeks and observed them for an additional 7 weeks. The dogs showed no evidence of central nervous system depression or stimulation. The dogs did have moderate ocular and nasal irritation. The authors observed hematological effects, including a decrease in hemoglobin, hematocrit, erythrocytes and increased hypochromia, polychromatophilia, and microcytosis in the erythrocytes in the exposed dogs (HEC=486 mg/cu.m) (Werner et al., 1943a). Werner et al. (1943b) exposed groups of 23 Wistar rats (both male and female) to 0 or 310 ppm ethylene glycol monomethyl ether (0 or 965 mg/cu.m, assuming 25C and 760 mm Hg) 7 hours/day, 5 days/week for 5 weeks, and observed some animals for an additional 3 weeks postexposure. Hematological effects included an increase in the percentage of juvenile granulocytes in the blood within 1 week of exposure, the replacement of bone marrow cells with fatty tissue, and a doubling of the hemosiderin content of the spleen (HEC=201 mg/cu.m) (Werner et al., 1943b).

Several acute inhalation studies in animals have shown that testicular effects occur rapidly after a short inhalation exposure to ethylene glycol monomethyl ether (Doe, 1984; Doe et al., 1983; Samuels et al., 1984; Miller et al., 1981). A 4-hour exposure of rats to concentrations of 600 ppm (1867 mg/cu.m) ethylene glycol monomethyl ether resulted in testicular atrophy. Male Wistar rats (10/group) exposed to 300 ppm ethylene glycol monomethyl ether (934 mg/cu.m) 6 hours/day for 10 consecutive days, had small, flaccid testes with pronounced atrophy of the

seminiferous tubules. Rats exposed to 100 ppm ethylene glycol monomethyl ether (311 mg/cu.m) did not experience these effects (Doe et al., 1983; Doe, 1984).

Exposure of rats to 50 ppm (156 mg/cu.m) ethylene glycol monomethyl ether 6 hours/day, 5 days/week for 1 or 2 weeks caused effects in the glial cells. The authors observed partial hindlimb paresis and a significant decrease in body weight during the second week of exposure in rats exposed to 400 ppm (1245 mg/cu.m) (Savolainen, 1980).

I.B.5. Confidence in the Inhalation RfC

Study — Medium

Database — Medium

RfC — Medium

Confidence in the key study is medium. The Miller et al. (1983) study is a well designed subchronic study in two species of animals (rat and rabbit) that histologically examined the testes, one of the target tissues for ethylene glycol monomethyl ether toxicity. Confidence in the database is medium. The LOAEL identified in the Miller et al. (1983) study was not corroborated by the Miller et al. (1982) study; however, a minimum threshold of effect was documented. The subchronic studies (Miller et al., 1982, 1983; Werner et al., 1943a,b) did not examine neurotoxicity endpoints and data on inhalation toxicity is reported indirectly. Reflecting medium confidence in the key study and medium confidence in the database, confidence in the inhalation RfC is medium.

I.B.6. EPA Documentation and Review of the Inhalation RfC

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — U.S. EPA, 1986

Agency Work Group Review — 12/19/1990

Verification Date — 12/19/1990

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for 2-Methoxyethanol conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

I.B.7. EPA Contacts (Inhalation RfC)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 2-Methoxyethanol

CASRN — 109-86-4

Not available at this time.

VI. Bibliography

Substance Name — 2-Methoxyethanol

CASRN — 109-86-4

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

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VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — 2-Methoxyethanol
CASRN — 109-86-4

Date	Section	Description
05/01/1991	I.B.	Inhalation RfC summary on-line

Date	Section	Description
10/28/2003	I.B.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — 2-Methoxyethanol

CASRN — 109-86-4

Last Revised — 05/01/1991

- 109-86-4
- Ethanol, 2-methoxy-
- AETHYLENGLYKOL-MONOMETHYLAETHER [German]
- BETA-METHOXYETHANOL
- Caswell No. 551
- Dowanol EM
- EGM
- EGME
- Ektasolve EM
- EPA Pesticide Chemical Code 042202
- Eter monometilico del etilenglicol [Spanish]
- Ethanol, 2-Methoxy-
- ETHER MONOMETHYLIQUE DE L'ETHYLENE-GLYCOL [French]
- Ether monomethylique de l'ethyleneglycol [French]
- ETHYLENE GLYCOL METHYL ETHER
- Ethylene Glycol Monomethyl Ether
- ETHYLENE GLYCOL, MONOMETHYL ETHER
- GLYCOL MONOMETHYL ETHER
- Glycolmethyl ether
- HSDB 97
- Methoxyethanol
- Methoxyhydroxyethane
- Methyl cellosolve
- METHYL ETHOXOL
- METHYL GLYCOL
- METHYL OXITOL
- Methylcelosolv [Czech]

- Methylglykol [German]
- METIL CELLOSOLVE [Italian]
- METOKSYETYLOWY ALKOHOL [Polish]
- MONOMETHYL ETHER of ETHYLENE GLYCOL
- Monomethyl Ethylene Glycol Ether
- NSC 1258
- POLY-SOLV EM
- UN 1188
- 1-HYDROXY-2-METHOXYETHANE
- 2-METHOXY-AETHANOL [German]
- 2-METHOXY-1-ETHANOL
- 2-Methoxyethanol
- 2-METOSSIETANOLO [Italian]