Health Based Guidance for Water
Health Risk Assessment Unit, Environmental Health Division
651-201-4899

Adopted as Rule: November 2023

Toxicological Summary for: Ethylene Glycol

CAS: **107-21-1**

Synonyms: Ethane-1,2-diol, Monoethylene glycol (MEG), 1,2-Ethanediol, Glycol

Acute Non-Cancer Health Risk Limit ($nHRL_{Acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 2000 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.33 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.038 L/kg-d)}^{**}}$$

= 1,736 rounded to **2,000 µg/L**

* Relative Source Contribution: MDH 2008, Section IV.E.1.

** The RfD is based on malformations that occur *in utero*, therefore, the intake rate for a pregnant woman is utilized rather than the default infant intake rate as described in the MDH 2008 SONAR (page 46). Effects relevant to post-natal development occurred at higher dose levels. As the short-term duration intake is based on pregnant women, not infants, a Relative Source Contribution of 0.2 is utilized. (Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3, and 3-5.)

Reference Dose/Concentration:	HED/Total UF = 9.83/30 = 0.33 mg/kg-d (CD-1 mice)
Source of toxicity value:	Determined by MDH in 2017
Point of Departure (POD):	75.6 mg/kg-d ($BMDL_{10}$; derived by ATSDR 2010, using data from Neeper-Bradley, 1995)
Dose Adjustment Factor (DAF):	0.13 (Body weight scaling, default) (MDH, 2017) (US EPA, 2011)
Human Equivalent Dose (HED):	POD x DAF = 75.6 mg/kg-d x 0.13 = 9.83 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Increased fetal skeletal malformations
Co-critical effect(s):	None
Additivity endpoint(s):	Developmental

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = 2000 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.33 mg/kg-d)}^{**} \text{ x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.038 L/kg-d)}^{**}}$$

= 1,736 rounded to **2,000 µg/L**

* Relative Source Contribution: MDH 2008, Section IV.E.1.

** The calculated Subchronic RfD (0.57 mg/kg-d) is higher than the Short-term RfD (0.33 mg/kg-d), which is based on developmental effects. The Subchronic RfD must be protective of all types of adverse effects that could occur as a result of subchronic exposure, including short-term effects (MDH, 2008). Therefore, the Short-term RfD is used in place of the calculated subchronic RfD and the water intake rate for a pregnant woman is used. (Intake rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3, and 3-5).

The calculated Subchronic nHRL, before consideration of the Short-term RfD and HRL, resulted in the same water guidance value after rounding to one significant digit. Therefore, the subchronic duration additivity endpoint of Renal (kidney) system is added to Developmental. **Additivity endpoints: Developmental, Renal (kidney) system**

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 2000 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.33 mg/kg-d)}^{**} \text{ x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.038 L/kg-d)}^{**}}$$

= 1,736 rounded to **2,000 µg/L**

* Relative Source Contribution: MDH 2008, Section IV.E.1

** The calculated Chronic RfD (0.44 mg/kg-d) is higher than the Short-term RfD (0.33 mg/kg-d), which is based on developmental effects. The Chronic RfD must be protective of all types of adverse effects that could occur as a result of chronic exposure, including short-term effects (MDH, 2008). Therefore, the Short-term RfD is used in place of the calculated Chronic RfD and the water intake rate for a pregnant woman is used. (Intake rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3, and 3-5)

The calculated Chronic nHRL, before consideration of the Short-term RfD and HRL, resulted in the same water guidance value after rounding to one significant digit. Therefore, the chronic duration additivity endpoints of Male Reproductive system and Renal (kidney) system are added to Developmental. **Additivity endpoints: Developmental, Male Reproductive system, Renal (kidney) system**

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification:	Not Classified
Slope factor (SF):	Not Applicable
Source of cancer slope factor (SF):	Not Applicable
Tumor site(s):	Not Applicable

Volatile: No

Summary of Guidance Value History:

In 1993/1994, MDH promulgated a Health Risk Limit (HRL) of 10,000 µg/L. In 2011, MDH derived acute, short-term, subchronic, and chronic noncancer Health Based Values (HBV) of 4,000 µg/L, 4,000 µg/L, 2,000 µg/L, and 2,000 µg/L, respectively. These HBVs were adopted as HRLs in 2011. In 2017, MDH re-evaluated the noncancer HRLs, resulting in the removal of the acute guidance, and the derivation of new noncancer short-term, subchronic, and chronic HBVs of 2,000 µg/L. The revisions were a result of 1) using MDH's most recent risk assessment methodology including the application of Human Equivalent Doses (HED) and updated intake rates; and 2) rounding to one significant digit. In 2020, MDH incorporated updated intake rates (USEPA 2019). Use of the updated intake rates did not result in any changes to the guidance values. In November 2023, the guidance values were adopted into Minnesota Rules, 4717.7860, as Health Risk Limits (HRLs).

Summary of toxicity testing for health effects identified in the Health Standards Statute (144.0751):

Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. MDH has considered the following information in developing health protective guidance.

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested for specific effect?	No	No	Yes	Yes	Yes
Effects observed?	-[1]	-[2]	Yes[3]	Yes[4]	Yes[5]

Comments on extent of testing or effects:

[1] Studies assessing endocrine function have not been conducted, however, secondary observations from histological examinations of endocrine organs in existing studies of ethylene glycol showed no effects in rats or mice.

[2] Repeat-dose studies assessing immunotoxicity and immune function have not been conducted. However, one study reported decreased leukocyte levels in rats at a dose 400 times higher than the short-term RfD.

[3] The short-term RfD is based on skeletal malformations observed in mouse fetuses following *in utero* exposure. Numerous developmental studies have been conducted, and mice have been shown to be

more sensitive than rats or rabbits regarding developmental effects. In addition to skeletal effects in mice, decreased fetal and pup body weights were observed at doses approximately 300 and 600 times higher than the short-term RfD.

[4] Reproductive and multi-generational studies have been conducted. Decreased reproductive success was observed at dose levels more than 600 times higher than the short-term RfD. Decreased sperm counts were observed at doses approximately 400 times higher than the short-term RfD, while sperm motility and morphology were altered at doses over 700 times higher than the short-term RfD.

[5] Following acute ingestion (poisoning incidents) of very high doses approximately 8000 times higher than the short-term RfD, ethylene glycol has a direct toxic effect on the nervous system with effects including ataxia, convulsion, and coma. In animal studies at doses 3000 times higher than the short-term RfD, calcium oxalate crystals have been observed in brain and nervous system tissue.

Resources Consulted During Review:

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