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

Web Publication Date: March 2025

Toxicological Summary for: Methyl Ethyl Ketone

CAS: **78-93-3**

Synonyms: Butan-2-one [IUPAC]; ethyl methyl ketone; 2-butanone; butanone; methyl acetone

Methyl ethyl ketone (MEK) is an industrial solvent nominated by the Minnesota Pollution Control Agency to the Minnesota Department of Health (MDH) for evaluation. During review, MDH examined the appropriateness of using a surrogate approach in order to derive health-based guidance for MEK. While oral toxicity data are lacking for MEK, there are data available for its metabolic precursor, 2-butanol, which shares similar physical/chemical properties and is rapidly and almost completely metabolized to MEK in the body. Therefore, MDH determined that 2-butanol is a suitable health-protective surrogate for MEK.

Acute Non-Cancer Health-Based Value (nHBVAcute) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health-Based Value (nHBVshort-term) = 400 µg/L

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

$$= \frac{\text{(0.61 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.290 L/kg-d)}^{**}}$$

= 421 rounded to **400 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**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 = 184/300 = 0.61 mg/kg-d (female Wistar rat)
Source of toxicity value:	Determined by MDH in 2024
Point of Departure (POD):	875 mg/kg-d ($BMDL_{0.5SD}$, multigenerational developmental study by Cox et al., 1975 using 2-butanol)
Dose Adjustment Factor (DAF):	0.21, Body weight scaling, study-specific
Human Equivalent Dose (HED):	POD x DAF = 875 mg/kg-d x 0.21 = 184 mg/kg-d
Total uncertainty factor (UF):	300

Uncertainty factor allocation:	3 for interspecies differences; 10 for intraspecies variability; and 10 for database uncertainty, including lack of MEK oral toxicity studies resulting in the use of the MEK metabolic precursor (2-butanol) as a surrogate
Critical effect(s):	Decreased litter pup body weight at post-natal day 4 in first generation offspring
Co-critical effect(s):	None
Additivity endpoint(s):	Developmental

Subchronic Non-Cancer Health-Based Value ($nHBV_{subchronic}$) = $nHBV_{short\text{-}term}$ = 400 µg/L

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

$$= \frac{\text{(0.61 mg/kg-d)}^{\dagger} \text{ x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 1,649 rounded to 2,000 µg/L

† The calculated Subchronic reference dose (RfD) (1.0 mg/kg-d) is higher than the Short-Term RfD (0.61 mg/kg-d), which is based on developmental effects. The Subchronic RfD must be protective of all types of adverse effects that could occur from Subchronic exposure, including short-term effects (MDH 2008, page 34). Therefore, the Short-Term RfD is used in place of the calculated Subchronic RfD for methyl ethyl ketone.

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3 and 3-5.

The Subchronic nHBV must be protective of shorter duration exposures that occur within the subchronic duration and, therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 400 µg/L.

Additivity endpoints: Developmental

Chronic Non-Cancer Health-Based Value ($nHBV_{chronic}$) = $nHBV_{short\text{-}term}$ = 400 µg/L

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

$$= \frac{\text{(0.61 mg/kg-d)}^{\ddagger} \text{ x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.045 L/kg-d)}^{**}}$$

= 2,711 rounded to 3,000 µg/L

‡ The calculated Chronic RfD (0.76 mg/kg-d) is higher than the Short-Term RfD (0.61 mg/kg-d), which is based on developmental effects. The Chronic RfD must be protective of all types of adverse effects that could occur

from chronic exposure, including short-term effects (MDH 2008, page 34). Therefore, the Short-Term RfD is used in place of the calculated Chronic RfD for methyl ethyl ketone.

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3 and 3-5.

The Chronic nHBV must be protective of shorter duration exposures that occur within the chronic duration and, therefore, the Chronic nHBV is set equal to the Short-term nHBV of 400 µg/L.

Additivity endpoints: Developmental; Renal (kidney) system

Cancer Risk Assessment Advice (cRAA) = Not Applicable

Volatile: Moderate

Summary of Guidance Value History:

A noncancer chronic HRL of 4,000 µg/L was promulgated in 1994. MDH derived short-term, subchronic, and chronic noncancer HBVs in 2025 that are lower than the 1994 HRL as a result of using MDH's most recent multiduration assessment methodology.

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?	No	No	Yes[1]	Yes[2]	Yes[3]

Comments on extent of testing or effects:

[1]Decreased body weight in offspring of female rats exposed to 2-butanol (a metabolic precursor to MEK) in drinking water during gestation provides the basis for MDH's Short-term reference dose (RfD). Inhalation studies with MEK and 2-butanol observed decreased fetal weights and increased skeletal abnormalities following exposure of female rats during pregnancy. This occurred at doses approximately 900-1,700 times greater than the Short-term RfD, which supports oral data suggesting 2-butanol can elicit developmental toxicity. There are no human-based developmental toxicity data available for MEK.

[2]Potential male reproductive toxicity was observed in rats following eight weeks' exposure to 2-butanol in drinking water at a dose approximately 1,500 times greater than the Short-term RfD. No studies examining reproductive toxicity from ingested MEK are available.

[3]Indicators of neurotoxicity (e.g., decreased activity, loss of muscle coordination, droopy eyelids) were observed in rats orally exposed to MEK at 1,300 times greater than the Short-term RfD. Decreased brain weights were observed in female rats exposed to MEK via inhalation at approximately 1,700 times greater than the Short-term RfD; other corresponding abnormalities were not observed. No other well-conducted studies in laboratory animals found evidence of neurological toxicity from inhaled or ingested MEK or 2-butanol.

Data from animals and humans suggest that MEK can increase the severity of neurotoxic effects from other solvents such as n-hexane. However, available studies do not provide adequate information to establish the lower limit of MEK exposure that may result in increased severity of effects by known neurotoxicants.

Resources Consulted During Review:

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