

Adopted as Rule: November 2023

## Toxicological Summary for: Acetone

CAS: 67-64-1

Synonyms: 2-propanone, propan-2-one, β-ketopropane, dimethyl ketone,  
dimethylformaldehyde, DMK

**Acute Non-Cancer Health Risk Limit (nHRL<sub>Acute</sub>) = Not Derived (Insufficient Data)**

**Short-term Non-Cancer Health Risk Limit (nHRL<sub>Short-term</sub>) = 5,000 µg/L**

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

$$= \frac{(3.1 \text{ mg/kg-d}) \times (0.5)^* \times (1000 \text{ µg/mg})}{(0.290 \text{ L/kg-d})^{**}}$$

$$= 5,344 \text{ rounded to } \mathbf{5,000 \text{ µg/L}}$$

\*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 = 312/100 = 3.1 mg/kg-d (F344N rats)
Source of toxicity value:	Determined by MDH in 2017
Point of Departure (POD):	1485 mg/kg-d (NOAEL, (NTP, 1991) (Dietz, 1991))
Dose Adjustment Factor (DAF):	0.21 (Body weight scaling, default) (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 1485 mg/kg-d x 0.21 = 312 mg/kg-d
Total uncertainty factor (UF):	100
Uncertainty factor allocation:	10 for intraspecies variability, and 10 for database uncertainty (lack of adequate developmental studies, including multigeneration studies, and neurotoxicity studies). No interspecies UF for toxicodynamics differences was applied as acetone plays a role in normal human metabolism and it is not anticipated that humans will be more sensitive to acetone than laboratory animals.
Critical effect(s):	Increased kidney weight (consistent with nephropathy seen in rats during the subchronic duration)
Co-critical effect(s):	None
Additivity endpoint(s):	Renal (kidney) system

**Subchronic Non-Cancer Health Risk Limit (nHRL<sub>Subchronic</sub>) = nHRL<sub>Short-term</sub> = 5,000 µg/L**

(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)  
(Subchronic Intake Rate, L/kg-d)

$$= \frac{(2.1 \text{ mg/kg-d}) \times (0.2)^* \times (1000 \text{ µg/mg})}{(0.074 \text{ L/kg-d})^{**}}$$

= 5,675 rounded to 6,000 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 = 207/100 = 2.1 mg/kg-d (F344N rat)  
Source of toxicity value: Determined by MDH in 2017  
Point of Departure (POD): 900 mg/kg-d (NOAEL (NTP, 1991) (Dietz, 1991))  
Dose Adjustment Factor (DAF): 0.23 (Body weight scaling, default) (USEPA, 2011) (MDH, 2017)  
Human Equivalent Dose (HED): POD x DAF = 900 mg/kg-d x 0.23 = 207 mg/kg-d  
Total uncertainty factor (UF): 100  
Uncertainty factor allocation: 10 for intraspecies variability, and 10 for database uncertainty (lack of adequate developmental studies, including multigenerational studies, neurotoxicity studies, and hematological studies). No interspecies UF of toxicodynamics differences was applied as acetone plays a role in normal human metabolism and it is not anticipated that humans will be more sensitive than laboratory animals.  
Critical effect(s): Nephropathy, increased relative kidney weight, changes in blood parameters (increased leukocytes, increased mean corpuscular hemoglobin, increased mean cell volume, decreased erythrocyte count, and decreased reticulocyte counts)  
Co-critical effect(s): Increased relative kidney weight, increased relative liver weight, increased incidence of hepatocellular hypertrophy, tubular degeneration in the kidneys  
Additivity endpoint(s): Hematological (blood) effects; Hepatic (liver) system; Renal (kidney) system

**The Subchronic nHRL must be protective of the acute and short-term exposures that occur within the subchronic period and therefore, the Subchronic nHRL is set equal to the Short-term nHRL of 5000 µg/L. Additivity endpoints: Renal (kidney) system**

**Chronic Non-Cancer Health Risk Limit (nHRL<sub>Chronic</sub>) = 3,000 µg/L**

$$\frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Chronic Intake Rate, L/kg-d})}$$
$$= \frac{(0.69 \text{ mg/kg-d}) \times (0.2)^* \times (1000 \text{ µg/mg})}{(0.045 \text{ L/kg-d})^{**}}$$
$$= 3,066 \text{ rounded to } \mathbf{3,000 \text{ µg/L}}$$

\*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 = 207/300= 0.69 mg/kg-d (F344N rat)
Source of toxicity value:	Determined by MDH in 2017
Point of Departure (POD):	900 mg/kg-d (NOAEL, (NTP, 1991) (Dietz, 1991), subchronic exposure)
Dose Adjustment Factor (DAF):	0.23 (Body weight scaling, default) (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 900 mg/kg-d x 0.23 = 207 mg/kg-d
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	10 for intraspecies variability, and 10 for database uncertainty (lack of adequate developmental studies, including multigenerational studies, neurotoxicity studies, and hematological studies), and 3 for subchronic to chronic extrapolation. No interspecies UF of toxicodynamics differences was applied as acetone plays a role in normal human metabolism and it is not anticipated that humans will be more sensitive than laboratory animals.
Critical effect(s):	Nephropathy, increased relative kidney weight, changes in blood parameters (increased leukocytes, increased mean corpuscular hemoglobin, increased mean cell volume, decreased erythrocyte count, and decreased reticulocyte counts)
Co-critical effect(s):	Increased relative kidney weight, increased relative liver weight, increased incidence of hepatocellular hypertrophy, tubular degeneration in the kidneys
Additivity endpoint(s):	Hematological (blood) effects; Hepatic (liver) 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:** Yes (moderate)

**Summary of Guidance Value History:**

In 1993/1994, MDH derived a chronic noncancer Health Risk Limit (HRL) of 700 µg/L. In 2011, MDH derived short-term, subchronic, and chronic noncancer Health Based Values (HBV) of 9,000, 8,000, and 4,000 µg/L, respectively. These HBVs were adopted as HRLs in 2011. In 2017, MDH re-evaluated the noncancer HRLs, resulting in new noncancer short-term, subchronic, and chronic HBVs of 5,000, 5,000, and 3,000 µg/L, respectively. The short-term, subchronic, and chronic values are lower as a result of 1) using MDH’s most recent risk assessment methodology, including Human Equivalence Doses (HED), and 2) rounding to one significant digit. In 2020 MDH incorporated updated intake rates (US EPA 2019). Use of the updated intake rates did not result in any changes to the guidance values. In November 2023, the updated HBVs 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	Yes	Yes	Yes	Yes
Effects observed?	-	No <sup>1</sup>	Yes <sup>2</sup>	Yes <sup>3</sup>	Yes <sup>4</sup>

**Comments on extent of testing or effects:**

<sup>1</sup> No immunotoxicity effects were observed in drinking water studies of mice at doses more than 200 fold higher than the chronic reference dose. Changes in thymus weight were observed in rats at doses nearly 300 fold higher than the short-term reference dose, but were not accompanied by other immunotoxicity effects.

<sup>2</sup> Offspring exposed to acetone through inhalation during gestation experienced decreased fetal weight and increased incidence of fetal malformations. During another inhalation study in mice, no developmental effects were seen in the offspring. A database uncertainty factor was incorporated into the derivation of short-term, subchronic, and chronic reference doses due to

lack of adequate multigenerational and developmental studies assessing developmental effects after oral exposure.

<sup>3</sup> Male rats exposed to acetone through drinking water for 13 weeks experienced an increase in relative testes weight, decreased caudal and epididymis weights, depressed sperm motility, and increased incidence of abnormal sperm at doses greater than 1000 fold higher than the chronic reference dose. No reproductive effects were seen when male rats were exposed to acetone in drinking water for six weeks prior to mating. A database uncertainty factor was incorporated into the derivation of short-term, subchronic, and chronic reference doses due to lack of an adequate multigenerational study assessing reproductive effects after oral exposure.

<sup>4</sup> A couple of neurotoxicity studies were conducted for oral exposure to acetone with only one reporting slightly altered vision in rats at a dose greater than 200 fold higher than the chronic reference dose. Excessive salivation was also observed in rats exposed to acetone in drinking water at a dose greater than 800 fold higher than the chronic reference dose, but it is unclear whether this is a neurological response or due to gavage administration. Narcotic-like effects have been reported after humans have inhaled or ingested acetone which include lethargy, minimal responsiveness, and comatose condition. A database uncertainty factor was incorporated into the derivation of short-term, subchronic, and chronic reference doses due to lack of adequate data addressing neurotoxic effects after oral exposure. Neurotoxicity observed in animals following inhalation of acetone include: inhibition of avoidance behavior, effects on fixed ratio and fixed interval response rates, and central nervous system depression measured by tests of unconditioned performance and reflexes.

#### **Resources Consulted During Review:**

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Groundwater Rules."

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Minnesota Department of Health (MDH) (2017). "MDH Health Risk Assessment Methods to Incorporate Human Equivalent Dose Calculations into Derivation of Oral Reference Doses. (May 2011, revised 2017)." From <https://www.health.state.mn.us/communities/environment/risk/docs/guidance/hedrefguide.pdf>

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U.S. Environmental Protection Agency (US EPA) (2011). "Recommended Use of Body Weight 3/4 as the Default Method in Derivation of the Oral Reference Dose." from <https://www.epa.gov/risk/recommended-use-body-weight-34-default-method-derivation-oral-reference-dose>

U.S. Environmental Protection Agency (EPA). (2019). Exposure Factors Handbook Chapter 3 Update 2019. Retrieved from <https://www.epa.gov/expobox/exposure-factors-handbook-chapter-3>

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