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

Adopted as Rule: November 2023

# Toxicological Summary for: Aminomethylphosphonic acid

CAS: **1066-51-9**

Synonyms: AMPA, 1-Aminomethylphosphonic acid; 1-Aminomethylphosphonate

*NOTE: AMPA (CAS# 1066-51-9), the glyphosate metabolite/degradate, is not to be confused with AMPA, the neurotoxic agent, which is a different chemical with CAS# 74341-63-2 with the same acronym. The neurotoxic AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate) is a specific agonist for the AMPA receptor where it mimics the effects of the neurotransmitter glutamate.*

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

**Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = Not Derived (Insufficient Data)**

**Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = 3,000 µg/L**

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

$$= \frac{\text{(0.96 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 2,594 rounded to **3,000 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: | HED/Total UF = 0.96 mg/kg-d (CD rats) |
| Source of toxicity value: | Determined by MDH in 2017 |
| Point of Departure (POD): | 400 mg/kg-d (administered dose NOAEL, Estes et al. 1979, Monsanto unpublished test report, as cited in WHO 1997, 2005) |
| Dose Adjustment Factor (DAF): | 0.24 (Body weight scaling, male rats (US EPA 2011, MDH 2017) |
| Human Equivalent Dose (HED): | POD x DAF = 400 mg/kg-d x 0.24 = 96 mg/kg-d |
| Total uncertainty factor (UF): | 100 |
| Uncertainty factor allocation: | 3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty (lack of multigenerational reproductive/developmental study) |
| Critical effect(s): | Decreased body weight gain, bladder urothelial hyperplasia, increased serum lactate dehydrogenase |
| Co-critical effect(s): | None |
| Additivity endpoint(s): | Hepatic (liver) system, Renal (kidney) system |

**Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 1,000 µg/L**

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

$$= \frac{(0.32 \text{ mg/kg-d}) \times (0.2)^{*} \times (1000 \text{ µg/mg})}{(0.045 \text{ L/kg-d})^{**}}$$

= 1,422 rounded to **1,000 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: | HED/Total UF = 0.32 mg/kg-d (CD rats) |
| Source of toxicity value: | Determined by MDH in 2017 |
| Point of Departure (POD): | 400 mg/kg-d (administered dose NOAEL, Estes et al. 1979, Monsanto unpublished subchronic study, as cited in WHO 1997, 2005) |
| Dose Adjustment Factor (DAF): | 0.24 (Body weight scaling, male rats (US EPA 2011, MDH 2017) |
| Human Equivalent Dose (HED): | POD x DAF = 400 mg/kg-d x 0.24 = 96 mg/kg |
| Total uncertainty factor (UF): | 300 |
| Uncertainty factor allocation: | 3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty (lack of multigenerational reproductive/development study), 3 for subchronic-to-chronic extrapolation |
| Critical effect(s): | Decreased body weight gain, bladder urothelial hyperplasia, increased serum lactate dehydrogenase |
| Co-critical effect(s): | None |
| Additivity endpoint(s): | 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: No**

**Summary of Guidance Value History:**
There are were current MDH HBVs or HRLs for AMPA prior to 2017. MDH developed a non-cancer pesticide rapid assessment value of 2,000 µg/L in 2016. The 2017 $nHBV_{Subchronic}$ was higher than the 2016 Pesticide Rapid Assessment due to use of a different intake rate. The 2017 $nHBV_{Chronic}$ was lower than the 2016 Pesticide Rapid Assessment Value due to use of a different relative source contribution and addition of a database uncertainty factor in the RfD derivation. 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 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 | No | No |
| Effects observed? | - | - [1] | Yes [2] | - | - [3] |

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

[1]AMPA has not been tested for immunotoxicity via oral ingestion. However, AMPA was negative for dermal sensitization in guinea pig tests.

[2]Decreased fetal body weight was reported in a gestational exposure study in rats at a dose which also produced overt maternal toxicity (including decreased bw gain, food consumption, soft stools, hair loss). This dose was 230 times higher than the subchronic RfD and findings were inconsistent with another developmental study that reported no maternal or fetal effects at a dose approximately 240 times higher than the subchronic RfD.

[3]AMPA has not been tested for neurotoxicity. However, there were no clinical signs of neurotoxicity in any of the short-term or subchronic tests in rats or dogs (i.e., no twitching, salivation or seizures, etc.).

**Resources Consulted During Review:**


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