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

Adopted as Rule: November 2023

Toxicological Summary for: Metolachlor OXA

CAS: **152019-73-3**

Synonyms: Oxanilic acid degradates of metolachlor, metolachlor OA, Metolachlor oxanilic acid

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

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 5,000 µg/L

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

$$= \frac{\text{(2.7 mg/kg-d) x (0.5)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.290 L/kg-d)}^{**}}$$

= 4,655 rounded to **5,000 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 = 265/100 = 2.7 mg/kg-d (beagle dog)
Source of toxicity value:	Determined by MDH in 2009
Point of Departure (POD):	500 mg/kg-d (NOAEL, Syngenta, 2004)
Dose Adjustment Factor (DAF):	0.53 (Body weight scaling, default) (US EPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 500 mg/kg-d x 0.53 = 265 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 two generation study)
Critical effect(s):	Changes in blood chemistry parameters without identified specific target organs
Co-critical effect(s):	None
Additivity endpoint(s):	None

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = $nHRL_{Short\text{-}term}$ = 5,000 µg/L

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

$$= \frac{\text{(2.7 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 7,297 rounded to 7,000 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 = 265/100 = 2.7 mg/kg-d (beagle dog)
Source of toxicity value:	Determined by MDH in 2009
Point of Departure (POD):	500 mg/kg-d (NOAEL, Syngenta, 2004)
Dose Adjustment Factor (DAF):	0.53 (Body weight scaling, default) (US EPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 500 mg/kg-d x 0.53 = 265 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 a two-generation study)
Critical effect(s):	Changes in blood chemistry parameters without identified specific target organs
Co-critical effect(s):	None
Additivity endpoint(s):	None

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 5,000 µg/L. Additivity endpoints: None

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

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

$$= \frac{\text{(0.27 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.045 L/kg-d)}^{**}}$$

= 1,200 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/Concentration:	HED/Total UF = 265/1000 = 0.27 mg/kg-d (beagle dog)
Source of toxicity value:	Determined by MDH in 2009
Point of Departure (POD):	500 mg/kg-d (NOAEL, Syngenta, 2004 (subchronic exposure))
Dose Adjustment Factor (DAF):	0.53 (Body weight scaling, default) (US EPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 500 mg/kg-d x 0.53 = 265 mg/kg-d
Total uncertainty factor (UF):	1000

Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, 10 for subchronic-to-chronic extrapolation, and 3 for database uncertainty (lack of two-generation study)
Critical effect(s):	Changes in blood chemistry parameters without identified specific target organs
Co-critical effect(s):	None
Additivity endpoint(s):	None

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:

A noncancer Health Based Value (HBV) of 1,000 µg/L was derived in 2004. Updated noncancer short-term, subchronic and chronic Health Risk Limits (HRL) of 3,000, 3,000, and 800 µg/L, respectively, were promulgated in 2011. In 2018, MDH re-evaluated the noncancer HRLs, resulting in updated values for the short-term, subchronic, and chronic durations of 5,000, 5,000, and 1,000 µg/L, respectively. The noncancer HBVs are higher as a result of 1) using MDH's most recent risk assessment methodology, 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 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?	-	-	No[1]	-	-

Comments on extent of testing or effects:

[1] The single available developmental study reported no treatment related effects to pregnant animals or fetuses at the highest dose tested, a dose 80 times higher than the short-term RfD. However, the database for the parent compound demonstrated that developmental toxicity observed in the two-generation reproductive/developmental study occurred at lower doses than the standard developmental study. As no two generation reproductive study has been conducted for metolachlor OXA, a database uncertainty factor was incorporated into the RfD derivation to address this data gap.

Resources Consulted During Review:

California Environmental Protection Agency Office of Environmental Health Hazard Assessment (OEHHA) (2017). "Metolachlor and Metolachlor Degradates Ethanesulfonic Acid and Oxanilic Acid in Groundwater." from https://oehha.ca.gov/media/downloads/pesticides/report/metolachlor05312017.pdf.

Minnesota Department of Health (MDH). (2008). Statement of Need and Reasonableness (SONAR), July 11, 2008. https://www.leg.state.mn.us/archive/sonar/SONAR-03733.pdf#page=2

Syngenta (personal communication from Patrick McCain, J., 2004). (2004). Metolachlor metabolite - oxanilic acid 90-day oral toxicity study in dogs. Central Toxicology Laboratory CTL/PTD1240/Regulatory/Report. March 16, 2004.

U.S. Environmental Protection Agency (EPA) (2000). "Data Evaluation Report, Metolachlor OA subchronic oral toxicity feeding - rat. MRID 44929509. January 2000. Reviewed by EPA in 2001.". from https://www3.epa.gov/pesticides/chem_search/cleared_reviews/csr_PC-108801_25-Apr-01_228.pdf.

U.S. Environmental Protection Agency (EPA) (2000). "Data Evaluation Report: Metolachlor OA Developmental Toxicity - Rat. MRID 44929510. Prepared 2000, Reviewed 2001." from https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/108800/108800-019.pdf.

U.S. Environmental Protection Agency (EPA) (2001). Memo: Metolachlor and s-Metolachlor - Report of the Hazard Identification Assessment Review Committee. Memo from Virginia Debozy dated September 28, 2001.

U.S. Environmental Protection Agency (EPA) (2001). Memo: Metolachlor and s-Metolachlor. Results of the Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Meeting held on 14-August-2001. Memo from Virginia Debozy dated August 14, 2001.

U.S. Environmental Protection Agency (EPA) (2001). Memo: Review of toxicity studies with Metolachlor/S-Metolachlor metabolites updated executive summaries for metolachlor DERs. Memo from Virginia Debozy dated December 12, 2001.

U.S. Environmental Protection Agency (EPA) (2002). Memo Revised Toxicology Chapter for Metolachlor/s-Metolachlor. PC Code 108801/108800. Memo from Virginia Debozy dated (May 13, 2002).

U.S. Environmental Protection Agency (EPA) (2002). Metolachlor: Revised HED Science Assessment for Tolerance Reassessment Eligibility Decision (RED). PC Code 108801. (May 23, 2002).

U.S. Environmental Protection Agency (EPA) (2003). Metolachlor. Revised HED Science Assessment for the Tolerance Reassessment Eligibility Decision, Including Various Pending Petitions. PC CODE 108801. Memo from Sherrie Kinard dated (February 12, 2003).

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