Toxicological Summary for: Metolachlor OXA

CAS: 152019-73-3
Synonyms: Oxanilic acid degradates of metolachlor, metolachlor OA, Metolachlor oxanilic acid

Acute Non-Cancer Health Based Value (nHBV_{Acute}) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Based Value (nHBV_{Short-term}) = 5,000 \, \mu g/L

\[
\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}
\]
\[
\text{(Short-term Intake Rate, L/kg-d)}
\]
\[
= (2.7 \, \text{mg/kg-d}) \times (0.5)^* \times \frac{1000 \, \mu g/mg}{(0.285 \, L/kg-d)^*}
\]
\[
= 4,737 \text{ rounded to } 5,000 \, \mu g/L
\]

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

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 Based Value (nHBV_{Subchronic}) = nHBV_{Short-term} = 5,000 \, \mu g/L

\[
\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}
\]
\[
\text{(Subchronic Intake Rate, L/kg-d)}
\]
\[
= (2.7 \, \text{mg/kg-d}) \times (0.2)^* \times \frac{1000 \, \mu g/mg}{(0.070 \, L/kg-d)^*}
\]

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= 7,714 rounded to 8,000 µg/L

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

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 nHBV must be protective of the acute, and short-term exposures that occur within the subchronic period and therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 5,000 µg/L. Additivity endpoints: None

Chronic Non-Cancer Health Based Value (nHBV\text{Chronic}) = 1,000 µg/L

\[
\frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Chronic Intake Rate, L/kg-d})} = \frac{(0.27 \text{ mg/kg-d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.044 \text{ L/kg-d})}\]

= 1,227 rounded to **1,000 µg/L**

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

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

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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 Based Value (cHBV) = 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.

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.

<table>
<thead>
<tr>
<th>Tested for specific effect?</th>
<th>Endocrine</th>
<th>Immunotoxicity</th>
<th>Development</th>
<th>Reproductive</th>
<th>Neurotoxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects observed?</td>
<td>-</td>
<td>-</td>
<td>No¹</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

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:


