



Minnesota
 Department
 of Health

Adopted as Rule: March 21, 2011

Chemical Name: Acetochlor OXA

CAS: 194992-44-4

Synonyms: Acetochlor Oxanilate Metabolite, R290130 **Acute Non-Cancer Health Risk Limit (nHRL_{acute}) = Insufficient data**

Short-term Non-Cancer Health Risk Limit (nHRL_{short-term}) = 200 µg/L

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

$$= \frac{(0.12 \text{ mg/kg/d}) \times (0.5) \times (1000 \text{ µg/mg})}{(0.289 \text{ L/kg-d})}$$

$$= 208 \text{ rounded to } \mathbf{200 \text{ µg/L}}$$

Reference Dose:	0.12 mg/kg-d (laboratory animal)
Source of toxicity value	MDH, 2009
Point of Departure:	370 mg/kg-d (LOAEL, MRID 45300506 as cited by EPA 2000a and 2006b)
Human Equivalent Dose Adjustment	Insufficient data
Total uncertainty factor	3000
UF allocation	10 for inter species extrapolation, 10 for intra species variation, 10 LOAEL-to-NOAEL, 3 for database insufficiency (lack of multigenerational reproductive study)
Critical effect(s):	Dose-related decrease in body weight gain, thyroid stimulating hormone (TSH), and total iodothyronine (tT3); increased relative thyroid weight
Co-critical effect(s):	None
Additivity endpoint(s):	Thyroid (E) Body weight effects in adults are not utilized for additivity)
Secondary effect(s):	None

Subchronic Non-Cancer Health Risk Limit (nHRL_{subchronic}) = 200 µg/L

$$= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Subchronic intake rate, L/kg/d})}$$

$$= \frac{(0.077 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.077 \text{ L/kg-d})}$$

$$= 200 \text{ µg/L}$$

Reference Dose:	0.077 mg/kg-d (laboratory animal)
Source of toxicity value	MDH, 2009
Point of Departure	77.2 mg/kg-d (NOAEL, MRID 45313805 as cited by EPA 2000 and 2006)

Human Equivalent Dose Adjustment: Insufficient data
 Total uncertainty factor: 1000
 UF allocation: 10 for inter species extrapolation, 10 for intra species variation, 10 for database insufficiency (lack of multigenerational reproductive study; insufficient studies for neurological and endocrine effects; lack of studies in a second species)
 Critical effect(s): Decreased food utilization, adult body weights and body weight gains
 Co-critical effect(s): Alterations in serum thyroid hormone levels
 Additivity endpoint(s): Thyroid (E)
 (Body weight effects in adults are not utilized for additivity)
 Secondary effect(s): None

Chronic Non-Cancer Health Risk Limit (nHRL_{chronic}) = 100 µg/L

$$= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Chronic intake rate, L/kg/d})}$$

$$= \frac{(0.026 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.043 \text{ L/kg-d})}$$

$$= 121 \text{ rounded to } \mathbf{100 \text{ µg/L}}$$

Reference Dose: 0.0257 mg/kg-d (laboratory animal)
 Source of toxicity value: MDH, 2009
 Point of Departure: 77.2 mg/kg-d (NOAEL, MRID 45313805 as cited by EPA 2000 and 2006)
 Human Equivalent Dose Adjustment: Insufficient data
 Total uncertainty factor: 3,000
 UF allocation: 10 for inter species extrapolation, 10 for intra species variation, 10 for database insufficiency (lack of multigenerational reproductive or developmental studies; insufficient studies for neurological and endocrine effects; lack of studies in a second species (dogs have been shown to be more sensitive)), and 3 for use of a subchronic study (based on consideration of a comparison of the 28 and 90 day studies, however, this comparison was considered inadequate to completely remove this UF).
 Critical effect(s): Decreased food utilization, adult body weights and body weight gains
 Co-critical effect(s): Alterations in serum thyroid hormone levels
 Additivity endpoint(s): Thyroid (E)
 (Body weight effects in adults are not utilized for additivity)
 Secondary effect(s): None

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification: Acetochlor OXA has not been classified as to its carcinogenic potential. However, EPA has indicated that it is unlikely to be carcinogenic (EPA 2004, EPA 2006b). The parent, acetochlor, is classified as “likely” to be carcinogenic and is considered to be a nonlinear carcinogen (i.e., there is a threshold level of exposure below which there is no cancer risk).

Volatile: No

Summary of changes since 1993/1994 HRL promulgation:

An HRL has not been established for acetochlor OXA. A chronic HBV of 50 µg/L was derived in 2006 based on a total UF of 10,000 and an intake adjustment factor of 3. The 2011 HRLs above are based on the 2009 HRL rules methodology (e.g., duration specific intake rates) and revised total uncertainty factor evaluations. As a result, the chronic 2011 HRL is 2-fold higher due to: 1) a lower POD; 2) a decrease in the magnitude of the subchronic-to-chronic UF from 10 to 3; 3) a lower intake rate; and 4) rounding to one significant figure.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Secondary Observations	No	Yes	No ³	Secondary Observations
Effects?	Yes ¹	--	No ²	--	Yes ⁴

Note: 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. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

- ¹ Alterations in thyroid hormone levels were reported at the lowest dose tested in a 28 day range-finding study and form the basis of the Short-term HRL. Alterations in thyroid hormone levels have also been reported for acetochlor ESA and the parent, acetochlor. Thyroid mechanism of action studies conducted on the parent, acetochlor, indicate that acetochlor disrupts thyroid-pituitary homeostasis via increased clearance of serum thyroxin (T4). The Subchronic study did not include an evaluation of thyroid hormone levels. The Subchronic HRL is based on the no adverse effect level (NOAEL) identified in the subchronic study and includes an uncertainty factor for database deficiency to address the need for additional testing on acetochlor OXA regarding altered thyroid hormone levels.
- ² A single developmental study has been conducted. No adverse developmental effects were reported at the highest dose tested. An increase in maternal mortality was observed in this study. Based on data for the parent, acetochlor, the 2 generation study reported significantly lower NOAEL/LOAEL value than the developmental study indicating that the standard developmental study protocol is not a sensitive test.
- ³ Male reproductive toxicity was a critical effect for the parent, acetochlor. The database uncertainty factor was, in part, applied to address the absence of a 2 generational reproductive study.
- ⁴ A dose-dependent increase in motor activity in males was observed in a 90 day study, however, this parameter was highly variable and only reached statistical significance (p<0.01) at the highest dose level. Researchers reported, but did not substantiate, that observations were within the range of historical controls. The nervous system has been identified as a chronic critical effect for the parent, acetochlor. The uncertainty factor for database deficiency is applied to the subchronic and chronic RfDs, in part, due to concerns that additional testing should be conducted.

References:

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