Adopted as Rule: August 2018

Toxicological Summary for: Acetochlor

CAS: **34256-82-1**

Synonyms: 2-Chloro-2'-methyl-6'-ethyl-N-ethoxymethyl-acetanilide; 2-Chloro-N-(ethoxymethyl)-6'-ethyl-o-acetotoluidide; 2-Chloro-N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)acetamide; 2'-Ethyl-6'-methyl-N-(ethoxymethyl)-2-chloroacetanilide

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

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 30 µg/L

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

$$= \frac{\text{(0.016 mg/kg-d) x (0.5)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.285 L/kg-d)}^{**}}$$

= 28.1 rounded to **30 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**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 = 0.016 mg/kg-d (Rat)
Source of toxicity value:	Determined by MDH in 2016
Point of Departure (POD):	22.4 mg/kg-d (NOAEL, Milburn 2001 (MRID 45357503) aci USEPA, 2006)
Dose Adjustment Factor (DAF):	0.22 (Body weight scaling, subchronic average female rat) (US EPA 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 22.4 mg/kg-d x 0.22 = 4.93 mg/kg-d
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	3 for interspecies differences (toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty (lack of developmental neurotoxicity studies and lack of short-term study in sensitive species (dog))

Critical effect(s):	Decreased pup body weight, decreased number of pups per litter, decreased pup spleen and brain weight
Co-critical effect(s):	Decreased mean pup body weight, increased UDGPT activity, increased T4, and decreased T3
Additivity endpoint(s):	Developmental, Hepatic (liver) system, Thyroid (E)

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = 30 µg/L

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

$$= \frac{\text{(0.012 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.070 L/kg-d)}}$$

= 34.3 rounded to **30 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**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 = 0.012 mg/kg-d (Beagle Dog)
Source of toxicity value:	Determined by MDH in 2016
Point of Departure (POD):	2 mg/kg-d (NOAEL, Broadmeadow 1988 (MRID 41565118), aci USEPA, 2006))
Dose Adjustment Factor (DAF):	0.59 (Body weight scaling, 1 year female dog) (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 2 mg/kg-d x 0.59 = 1.18 mg/kg-d
Total uncertainty factor (UF):	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, 3 for database uncertainty (for lack of developmental neurotoxicity studies
Critical effect(s):	Increased salivation, increased incidence of renal interstitial nephritis, testicular histopathology (testicular degeneration and hypospermia), liver glycogen depletion
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system, Male Reproductive system, Nervous system, Renal (kidney) system

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 20 µg/L

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

(Chronic Intake Rate, L/kg-d)

$$= \frac{(0.0039 \text{ mg/kg-d}) \times (0.2)^{*} \times (1000 \text{ µg/mg})}{(0.044\text{L/kg-d})^{**}}$$

= 18.2 rounded to **20 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**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 = 0.0039 mg/kg-d (Beagle Dog)
Source of toxicity value:	Determined by MDH in 2016
Point of Departure (POD):	2 mg/kg-d (NOAEL, Broadmeadow 1988 (MRID 41565118) (subchronic exposure), aci USEPA, 2006)
Dose Adjustment Factor (DAF):	0.59 (Body weight scaling, 1 year female dog) (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 2 mg/kg-d x 0.59 = 1.18 mg/kg-d
Total uncertainty factor (UF):	300
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for extrapolation from subchronic to chronic
Critical effect(s):	Increased salivation, increased incidence of renal interstitial nephritis and chronic vasculitis, testicular histopathology (testicular degeneration and hypospermia), liver glycogen depletion
Co-critical effect(s):	Increased incidence of bronchiolar hyperplasia and renal tubular hyperplasia, decreased body weight gain
Additivity endpoint(s):	Hepatic (liver) system, Male Reproductive system, Nervous system, Renal (kidney) system, Respiratory system

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification:	Suggestive Evidence of Carcinogenic Potential by all routes (USEPA, 2013)
Slope factor (SF):	Not Applicable
Source of cancer slope factor (SF):	Not Applicable
Tumor site(s):	Nasal, lung, thyroid, and histiocytic sarcoma

Statement for non-linear carcinogens:

Acetochlor is a nonlinear carcinogen and the chronic RfD is considered to be protective against cancer.

Volatile: No

Summary of Guidance Value History:

A noncancer chronic Health Based Value (HBV) of 10 µg/L was derived in 1995. In 2009, acute, short-term, subchronic HRLs of 40 µg/L and a chronic HRL of 9 µg/L were derived. In 2016, MDH re-evaluated the non-cancer HRLs, resulting in new noncancer short-term, and subchronic HBVs of 30 µg/L and a chronic HBV of 20 µg/L. The acute guidance was removed, the short-term and subchronic values were lower, and the chronic value was higher as a result of 1) using MDH's most recent risk assessment methodology, including the application of Human Equivalence Doses and 2) rounding to one significant digit. The 2016 guidance was adopted as HRLs in 2018.

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?	Yes	No	Yes	Yes	No
Effects observed?	Yes[1]	-	Yes[2]	Yes[3]	-[4]

Comments on extent of testing or effects:

[1] Increased adrenal and thyroid organ weights have been reported following exposure to doses up to 2 to 4 fold higher than the administered subchronic/chronic critical study LOAEL. Thyroid mechanism of action studies at high doses suggest that acetochlor disrupts the thyroid-pituitary homeostasis via increased hepatic UDPGH-mediated increased clearance of thyroxin (T4). Changes in circulating thyroid hormone levels were observed at these higher doses. These effects have been identified as co-critical effects for the short-term exposure duration.

[2] Developmental effects have been listed as an endpoint in several studies. Decreased pup weight, decreased litter size (suggestive of fetal loss) and changes in spleen and brain weights were observed at the administered acute/short-term critical study LOAEL. These effects have been identified as acute/short-term critical effects.

[3] Histological changes in the epididymides and testes, hypospermia, degeneration of seminiferous tubules, decreased relative testes weight, and testicular atrophy were observed at the administered subchronic/chronic critical study LOAEL. Male reproductive effects are listed as a subchronic/chronic critical effect.

[4] Neurological symptoms (e.g., salivation) were reported at the subchronic/chronic critical study LOAEL. These effects are listed as a subchronic/chronic critical effect. Severe neurological effects (e.g., ataxia) were observed at administered dose levels 5-fold higher. Developmental

and short-term studies did not include adequate assessments of neurotoxicity. As a result a database uncertainty factor of 10 was incorporated into the derivation of the short-term RfD and subchronic RfD.

Resources Consulted During Review:

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U.S. Environmental Protection Agency (USEPA). (2006). "Acetochlor Revised HED Chapter of the Tolerance Reassessment Eligibility Decision (TRED) Document) ", from https://www.regulations.gov/document?D=EPA-HQ-OPP-2005-0227-0024.

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