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**Chemical Name: Acetochlor**

**CAS Number: 34256-82-1**

**Synonyms: 2-Chloro-N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)acetamide**

**Acute Non-Cancer Health Risk Limit (nHRL<sub>acute</sub>) = 40 ug/L**

$$\begin{aligned} &= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Acute intake rate, L/kg/d})} \\ &= \frac{(0.021 \text{ mg/kg/d}) \times (0.5) \times (1000 \text{ ug/mg})}{(0.289 \text{ L/kg-d})} \\ &= 36.33 \text{ rounded to } \mathbf{40 \text{ug/L}} \end{aligned}$$

Reference Dose:	0.021 mg/kg-d	(laboratory animal)
Source of toxicity value:	MDH 2007	
Point of Departure:	21.2-mg/kg-d	(NOAEL, Milburn, 2001 as cited by EPA 2006)
Human Equivalent Dose Adjustment:	None (Insufficient information)	
Total uncertainty factor:	1000	
UF allocation:	10 fold for interspecies extrapolation, 10 for intraspecies variability and 10 for database insufficiencies due to lack of a developmental neurotoxicity study and short-term studies in the more sensitive species, the dog.	
Critical effect(s):	decreased pup body weight, decreased pups per litter, decreased pup spleen and brain weight.	
Co-critical effect(s):	None	
Additivity endpoint(s):	Developmental (decreased body weight, increased mortality, spleen and brain weight)	
Secondary effect(s):	None	

**Short-term Non-Cancer Health Risk Limit (nHRL<sub>short-term</sub>) = 40 ug/L**

$$\begin{aligned} &= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Short-term intake rate, L/kg/d})} \\ &= \frac{(0.021 \text{ mg/kg/d}) \times (0.5) \times (1000 \text{ ug/mg})}{(0.289 \text{ L/kg-d})} \\ &= 36.33 \text{ rounded to } \mathbf{40 \text{ ug/L}} \end{aligned}$$

Reference Dose:	0.021 mg/kg-d	(laboratory animal)
Source of toxicity value:	MDH 2007	
Point of Departure:	21.2-mg/kg-d	(NOAEL, Milburn, 2001 as cited by EPA 2006)
Human Equivalent Dose Adjustment:	None (Insufficient information)	
Total uncertainty factor:	1000	
UF allocation:	10 fold for interspecies extrapolation, 10 for intraspecies variability and 10 for database insufficiencies due to lack of a developmental neurotoxicity study and short-term studies in the more sensitive species, the dog.	
Critical effect(s):	decreased pup body weight, decreased pups per litter, decreased pup spleen and brain weight.	
Co-critical effect(s):	None	
Additivity endpoint(s):	Developmental (decreased body weight, increased mortality, spleen and brain weight)	
Secondary effect(s):	increased liver and thyroid weight, changes in thyroid hormone levels	

**Subchronic Non-Cancer Health Risk Limit (nHRL<sub>subchronic</sub>) = nHRL<sub>short-term</sub> = 40 ug/L**

$$\begin{aligned} &= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Subchronic intake rate, L/kg/d})} \\ &= \frac{(0.02 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ ug/mg})}{(0.077 \text{ L/kg-d})} \\ &= 51.94 \text{ rounded to } \mathbf{50 \text{ ug/L}} \end{aligned}$$

Toxicity value:	0.02 mg/kg-d	(laboratory animal)
Source of toxicity value:	MDH 2007	
Point of Departure:	2 mg/kg-d	(NOAEL, Broadmeadow 1988 as cited by EPA 2006)
Human Equivalent Dose Adjustment:	None (Insufficient information)	
Total uncertainty factor:	100	
UF allocation:	10 fold for interspecies extrapolation, 10 for intraspecies variability	

Critical effect(s): testicular histopathology (tubular degeneration, hypospermia of the epididymides), hepatic effects (reduced glycogen), renal histopathology (interstitial nephritis, chronic vasculitis) and increased salivation in males

Co-critical effect(s): None

Additivity endpoint(s): Hepatic (Liver) system, Renal (Kidney) system, Male reproductive system, Nervous system

Secondary effect(s): None

**The subchronic HRL must be protective of 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 40 ug/L. Additivity Endpoint: Developmental.**

**Chronic Non-Cancer Health Risk Limit (nHRL<sub>chronic</sub>) = 9 ug/L**

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

$$= \frac{(0.002 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ ug/mg})}{(0.043 \text{ L/kg-d})}$$

$$= 9.30 \text{ rounded to } \mathbf{9 \text{ ug/L}}$$

Reference Dose: 0.002 mg/kg-d (human or laboratory animal)

Source of toxicity value: MDH 2007

Point of Departure: 2 mg/kg-d (NOAEL, Broadmeadow 1988 as cited by EPA 2006)

Human Equivalent Dose Adjustment: None (Insufficient information)

Total uncertainty factor: 1000

UF allocation: 10 fold for interspecies extrapolation, 10 for intraspecies variability and 10 for subchronic-to-chronic

Critical effect(s): testicular histopathology (tubular degeneration, hypospermia of the epididymides), hepatic effects (reduced glycogen), renal histopathology (interstitial nephritis, chronic vasculitis) and increased salivation in males

Co-critical effect(s): bronchiolar hyperplasia and renal tubular hyperplasia

Additivity endpoint(s): Hepatic (Liver) System, Renal (Kidney) system, Male reproductive system, Nervous system, Respiratory System

Secondary effect(s): increased thyroid weight (adults and offspring)

**Cancer Health Risk Limit (cHRL) = Not Applicable<sup>1</sup>**

Cancer classification: “Suggestive Evidence of Carcinogenic Potential”  
Slope factor: withdrawn, nonlinear approach recommended (EPA 2006)  
Source of slope factor: not available  
Tumor site(s): Nasal, lung, thyroid, liver and histiocytic sarcoma

<sup>1</sup>Acetochlor is a nonlinear carcinogen, and the RfD and subsequent chronic noncancer HRL of 9 ug/L is considered to be protective against cancer.

**Volatile: No**

**Summary of changes since 1993/1994 HRL promulgation:**

There is no 1993/94 HRL value for acetochlor. The chronic noncancer HRL (9 ug/L) represents a new HRL value and is slightly lower than the 1995 chronic noncancer Health Based Value (10 ug/L). The chronic HRL is also 4.5-fold higher than the 2006 cancer Health Based Value (2 ug/L) as the result of applying a nonlinear cancer assessment methodology rather than a linear approach as recommended by EPA.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Yes	No	Yes	Yes	No
Effects?	Yes <sup>1</sup>	--	Yes <sup>2</sup>	Yes <sup>3</sup>	Secondary observations <sup>4</sup>

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.

-- indicates that no specific tests for that effect were conducted, and that effect was not observed as a secondary effect in any other study used in the HRL evaluation.

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

<sup>1</sup> Increased adrenal and thyroid organ weights have been reported following exposure to doses up to 2-4-fold higher than the 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 secondary effects for subchronic and chronic exposure durations.

<sup>2</sup> Developmental effects has been list 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 acute/short-term critical study LOAEL. These effects have been identified as acute/short-term critical effects.

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

<sup>4</sup> Neurological symptoms (e.g., salivation) 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 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 acute and short-term RfD.

## References:

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