



[Web Publication Date:](#) March 21, 2011

Chemical Name: Acetochlor ESA

CAS #: 187022-11-3

Synonyms: Acetochlor Ethane Sulfonic Acid; CP92429-2, MON 53754

Acute Non-Cancer Health Risk Limit (nHRL_{acute}) = Insufficient data

Short-term Non-Cancer Health Risk Limit (nHRL_{short-term}) = 600 µg/L

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

$$= \frac{(0.37 \text{ mg/kg/d}) \times (0.5) \times (1000 \text{ µg/mg})}{(0.289 \text{ L/kg-d})}$$

$$= 640 \text{ rounded to } \mathbf{600 \text{ µg/L}}$$

Reference Dose: 0.37 mg/kg-d (laboratory animal)

Source of toxicity value: MDH, 2009

Point of Departure: 370.3 mg/kg-d (minimal LOAEL, MRID 45300503 as cited by EPA 2000a and 2006b)

Human Equivalent Dose Adjustment: Insufficient data

Total uncertainty factor: 1000

UF allocation: 10 for inter species extrapolation, 10 for intra species variation, 3 minimal LOEL-to-NOAEL, 3 for database insufficiency (lack of multigenerational reproductive or developmental studies)

Critical effect(s): Dose-related increase in thyroid stimulating hormone (TSH) and free thyroxine (T4)

Co-critical effect(s): None

Additivity endpoint(s): Thyroid (E)

Secondary effect(s): None

Subchronic Non-Cancer Health Risk Limit (nHRL_{subchronic}) = 600 µg/L

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

$$= \frac{(0.23 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.077 \text{ L/kg-d})}$$

$$= 597 \text{ rounded to } \mathbf{600 \text{ µg/L}}$$

Reference Dose: 0.23 mg/kg-d (laboratory animal)
Source of toxicity value: MDH, 2009
Point of Departure: 225.4 mg/kg-d (NOAEL, MRID 45313801 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 or developmental studies; 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}) = 300 µg/L

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

$$= \frac{(0.075 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.043 \text{ L/kg-d})}$$

$$= 349 \text{ rounded to } \mathbf{300 \text{ µg/L}}$$

Reference Dose: 0.075 mg/kg-d (laboratory animal)
Source of toxicity value: MDH, 2009
Point of Departure: 225.4 mg/kg-d (NOAEL, MRID 45313801 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 ESA 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 Guidance Value History:

There is no 1993/94 HRL for acetochlor ESA. 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 6-fold higher due to: 1) a decrease in the magnitude of the subchronic-to-chronic UF from 10 to 3; 2) a lower intake rate; and 3) 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	No ²	No ³	Yes
Effects?	Yes ¹	--	--	--	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 OXA 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 ESA regarding altered thyroid hormone levels.
- ² No developmental study has been conducted. Registrant recommended that the OPP consider thealachlor ESA developmental study in rats as evidence that development is not a sensitive endpoint. The developmental study on the parent, acetochlor, identified LOAELs of 400-600 mg/kg-d and NOAELs of 150 – 200 mg/kg-d, based on signs of clinical toxicity and decreased weight gain in pregnant animals, increased resorptions and decreased fetal weights. However, the multiple generation study on the parent identified significantly lower NOAEL/LOAEL values (21-22/66-71 mg/kg-d), indicating that the standard developmental study protocol is not a sensitive test. A database uncertainty factor was incorporated into the derivation of the RfD, in part, due to the lack of a multigeneration reproductive study.
- ³ Male reproductive toxicity (testicular degeneration and decreased testes weight) was a critical effect for the parent, acetochlor. Alterations in testes weights were reported in the short-term range finding study but not in the 90 day study. A database uncertainty factor was incorporated into the derivation of the RfD, in part, due to concerns that additional testing should be conducted.
- ⁴ A functional observation battery for neurotoxicity was conducted and histopathology of the sciatic nerve was assessed in a 90 study for general toxicity. There were possible signs of neurotoxicity, but none showed dose dependency. Neurological effects were a sensitive endpoint for the parent, acetochlor. A database uncertainty factor was incorporated into the derivation of the subchronic and chronic RfDs, in part, due to concerns that additional testing should be conducted.

References:

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. <http://www.atsdr.cdc.gov/mrls.html>

California Environmental Protection Agency, OEHHA Toxicity Criteria Database. <http://www.oehha.ca.gov/risk/ChemicalDB/index.asp>; <http://www.oehha.ca.gov/risk/pdf/cancerpotalpha81005.pdf>

Environmental Protection Agency (EPA). Integrated Risk Information System.

EPA 1981. Data Evaluation Record. Acetochlor Ethane Sulfonate Acid Acute Toxicity study. Citation: Birch, M.S., 1981 Acute toxicity studies (ODES) on acetochlor ethane sulfonic acid (ESA), CP 92429-2. Younger Laboratories Incorporated, 123 Cliff Cave Road, St. Louis, MO 63129. report/Project No. YO-81-056, July 8, 1981. MMRID 45300502. Unpublished. EPA DER TXR# 0050658

EPA 1997a. Health Effects Assessment Summary Tables (HEAST). July 1997.

EPA 1997b. Data Evaluation Record. Acetochlor Ethane Sulfonate Acute Toxicity Study. Citation: Lees, D. (1997). Sulphonic Acid (R290131): Acute Oral Toxicity to the Rat, performed at (Zeneca's) Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire (UK), Study No. AR6415/Report No. CTL/P/5648, MRID 44632704. Unpublished.

EPA 2000a. Data Evaluation Record. Acetochlor Ethane Sulfonate Acid Metabolite 4-week Range-finding study. Citation: Lees, D. (2000) R290131: 28 day dietary toxicity study in rats. Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire (UK), laboratory report No: CTL/KR1350/REG/REPT, Jan 10, 2000. MRID 45300503.

EPA 2000b. Data Evaluation Record. Acetochlor ESA Metabolite 90 day study. Citation: Lees, D. (2000) R290131: 90 day dietary toxicity study in rats. Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire (UK), laboratory report No: CTL.PR1147/REG/REPT May 19, 2000. MRID 45313801 unpublished.

EPA 2004. Acetochlor. Report of the Metabolism Assessment Review Committee. August 31, 2004. Alberto Protzel. TXR No. 0052813.

EPA 2006a. Office of Drinking Water. Drinking Water Standards and Health Advisories (August, 2006) <http://www.epa.gov/waterscience/criteria/drinking/dwstandards.pdf>

EPA 2006b. Acetochlor: Revised HED Chapter of the Tolerance Reassessment Eligibility Decision (TRED) Document. Dated March 1, 2006. Document ID EPA-HQ-OPP-2005-0227-0024 (search for Docket number EPA-HQ-OPP-2005-0227). <http://www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d=EPA-HQ-OPP-2005-0227>

EPA Region 3. Risk Based Concentration. (click on RBC Tables PDF link) <http://www.epa.gov/reg3hwmd/risk/human/rbc/rbc1006.pdf>

EPA Region 9. Preliminary Remediation Goal. (click on Region 9 PRGs 2004 Table link) <http://www.epa.gov/region09/waste/sfund/prg/files/04prgtable.pdf>

Gadagui B, A Maier, M Dourson, A Parker, A Willis, JP Christopher, L Hicks, S Ramasamy, SM Roberts. 2010. Derived Reference Doses (RfDs) for the environmental degradates of the herbicides alachlor and acetochlor: Results of an independent expert panel deliberation. Regulatory Toxicology and Pharmacology. Doi:10.1016/j.yrtph.2010.02.010

International Agency for Research on Cancer (IARC). Agents Reviewed by the IARC Monographs. <http://monographs.iarc.fr/ENG/Classification/Listagentsalphorder.pdf>

Oak Ridge National Laboratory. Screening Levels for Chemical Contaminants. <http://epa-prgs.ornl.gov/chemicals/download.shtml>

Syracuse Research PhysProp Database. <http://www.syrres.com/esc/physdemo.htm>

WHO Recommended Classification of Pesticides by Hazard. 2004.

http://www.who.int/ipcs/publications/pesticides_hazard_rev_3.pdf

World Health Organization. Guidelines for Drinking-Water Quality. Chapter 12

Chemical Fact Sheets. http://www.who.int/water_sanitation_health/dwq/gdwq0506_12.pdf