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Chemical Name: Metolachlor ESA

CAS: 171118-09-5

Synonyms: Ethanesulfonate degradate of metolachlor; CGA-354743

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

Short-term Non-Cancer Health Risk Limit (nHRL_{short-term}) = Insufficient Data (Not Derived)

Subchronic Non-Cancer Health Risk Limit (nHRL_{subchronic}) = 4000 µg/L

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

$$= \frac{(1.7 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.077 \text{ L/kg-d})}$$

$$= 4415 \text{ rounded to } \mathbf{4000 \text{ µg/L}}$$

Reference Dose: 1.7 mg/kg-d (laboratory animal)

Source of toxicity value: MDH, 2009

Point of Departure: 500 mg/kg-d (NOAEL, based on a 90 day subchronic study in dogs, MRID 44931709 Data Evaluation Report submitted to EPA 2001)

Human Equivalent Dose Adjustment: Insufficient data

Total uncertainty factor: 300

UF allocation: 10 interspecies extrapolation, 10 intraspecies variability and 3 database insufficiencies (e.g., lack of a 2 generation reproductive study)

Critical effect(s): Increased levels of serum liver enzymes and statistically significant trend in increased liver weight.

Co-critical effect(s): None

Additivity endpoint(s): Hepatic (liver) system

Secondary effect(s): None

Chronic Non-Cancer Health Risk Limit (nHRL_{chronic}) = 800 µg/L

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

$$= \frac{(0.17 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.043 \text{ L/kg-d})}$$

$$= 790 \text{ rounded to } \mathbf{800 \text{ µg/L}}$$

Reference Dose: 0.17 mg/kg-d (laboratory animal)

Source of toxicity value: MDH, 2009

Point of Departure: 500 mg/kg-d (NOAEL, based on a 90 day subchronic study in dogs, MRID 44931709 a Data Evaluation Report submitted to EPA 2001)

Human Equivalent Dose Adjustment: Insufficient data

Total uncertainty factor: 3000

UF allocation: 10 interspecies extrapolation, 10 intraspecies variability, 10 use of a subchronic study (inadequate information for comparing effects across exposure duration - default value was used), and 3 database insufficiencies (e.g., lack of a 2 generation reproductive study)

Critical effect(s): Increased levels of serum liver enzymes and statistically significant trend in increased liver weight.

Co-critical effect(s): None

Additivity endpoint(s): Hepatic (liver) system

Secondary effect(s): None

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification: information on carcinogenicity is unavailable¹

Slope factor: None

Source of slope factor: None

Tumor site(s): Unavailable

¹Nonlinear approach is recommended for the parent compound (metolachlor). MDH considers the RfD protective of cancer.

Volatile: No

Summary of Guidance Value History:

There is no 1993/94 HRL for metolachlor ESA. The chronic 2011 nHRL (800 µg/L), is slightly lower than the HBV issued in 2004 (1000 µg/L) due to: 1) incorporation of a database uncertainty factor; 2) utilization of a lower intake rate; and 3) rounding to one significant digit.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	No ¹	Yes	No ²	No
Effects?	--	--	No ²	--	--

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:

The database for metolachlor ESA is limited (one developmental study in rats, one subchronic study in rats and one subchronic study in dogs). The database for the parent compound (metolachlor) is comprehensive and includes reproductive, numerous developmental, and chronic (oncogenicity) studies.

¹ Dermal sensitization studies have been done, and some sensitization is observed. However, there is no indication of toxicity to the immune system.

² The single available developmental study reported no treatment related effects to pregnant animals or fetuses at the highest dose tested. This dose level is higher than the critical study LOAEL. The database for the parent compound demonstrated that developmental toxicity observed in the 2 generation reproductive study occurred at lower doses than the standard developmental study. No 2 generation reproductive study has been conducted for metolachlor ESA. A database uncertainty factor was incorporated into the RfD derivation to address this data gap.

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