

Toxicological Summary for: Alachlor

CAS: **15972-60-8**

Synonyms: 2-Chloro-N-(2,6-diethylphenyl)-N-(methoxymethyl)acetamide; Methoxymethyl-2',6'-diethylanilide chloroacetate;

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

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

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

$$= \frac{(0.077 \text{ mg/kg-d}) \times (0.5)^* \times (1000 \text{ µg/mg})}{(0.285 \text{ L/kg-d})^{**}}$$

$$= 135 \text{ rounded to } \mathbf{100 \text{ µg/L}}$$

*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 = 0.077 mg/kg-d (Sprague Dawley Rat)
Source of toxicity value:	Determined by MDH in 2016
Point of Departure (POD):	10 mg/kg-d (NOAEL, Schroeder et al., 1981 (MRID 00075062) aci USEPA, 1998)
Dose Adjustment Factor (DAF):	0.23 (Body weight scaling, subchronic Female Sprague Dawley Rat) (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 10 mg/kg-d x 0.23 = 2.3 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Decreased kidney weight in pups and adult animals, nephritis, kidney damage
Co-critical effect(s):	None
Additivity endpoint(s):	Developmental, Renal (kidney) system

Subchronic Non-Cancer Health Risk Limit (nHRL_{Subchronic}) = 60 µg/L

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

$$= \frac{(0.020 \text{ mg/kg-d}) \times (0.2)^* \times (1000 \text{ µg/mg})}{(0.285 \text{ L/kg-d})^{**}}$$

(0.070 L/kg-d)**

= 57.1 rounded to **60 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 = 0.020 mg/kg-d (Beagle Dog)
Source of toxicity value: Determined by MDH in 2016
Point of Departure (POD): 1 mg/kg-d (NOAEL, Naylor et al., 1984 (MRID 00148923) aci USEPA, 1998)
Dose Adjustment Factor (DAF): 0.61 (Body weight scaling, 1 year male dog) (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED): POD x DAF = 1 mg/kg-d x 0.61 = 0.61 mg/kg-d
Total uncertainty factor (UF): 30
Uncertainty factor allocation: 3 for interspecies differences (toxicodynamics), 10 for intraspecies variability
Critical effect(s): Hemosiderosis of the kidney and spleen
Co-critical effect(s): Increased liver weight
Additivity endpoint(s): Hematological (blood) system, Hepatic (liver) system, Renal (kidney) system

Chronic Non-Cancer Health Risk Limit (nHRL_{Chronic}) = 9 µg/L

$$\frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Chronic Intake Rate, L/kg-d})}$$
$$= \frac{(0.0020 \text{ mg/kg-d}) \times (0.2)^* \times (1000 \text{ µg/mg})}{(0.044 \text{ L/kg-d})^{**}}$$
$$= 9.1 \text{ rounded to } \mathbf{9 \text{ µg/L}}$$

*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 = 0.0020 mg/kg-d (Beagle Dog)
Source of toxicity value: Determined by MDH in 2016
Point of Departure (POD): 1 mg/kg-d (NOAEL, Naylor et al., 1984 (MRID 00148923) aci (USEPA, 1988) subchronic study)
Dose Adjustment Factor (DAF): 0.61 (Body weight scaling, 1 year male dog) (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED): POD x DAF = 1 mg/kg-d x 0.61 = 0.61 mg/kg-d
Total uncertainty factor (UF): 300
Uncertainty factor allocation: 3 for interspecies differences (toxicodynamics), 10 for intraspecies variability, and 10 for extrapolation from subchronic to chronic duration
Critical effect(s): Hemosiderosis of the kidney and spleen,
Co-critical effect(s): Increased liver weight
Additivity endpoint(s): Hematological (blood) system, Hepatic (liver) system, Renal (kidney) system

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification: Likely to be carcinogenic at high doses, but not likely at low doses, by all exposure routes (USEPA, 1988, 2007)

Slope factor (SF): 0.08 per (mg/kg-d)⁻¹, however a nonlinear approach is recommended (USEPA, 1988)

Source of cancer slope factor (SF): USEPA, 1998

Tumor site(s): Nasal, stomach, and thyroid tumors

Statement for non-linear carcinogens:

Alachlor 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 Risk Limit (HRL) of 4 µg/L was promulgated in 1993/1994. In 2007, as required by a Legislative Session Law (Chapter 147, Article 17, section 2), the HRL was set equal to the MCL of 2 µg/L until MDH conducted a full review. Later in 2007 MDH derived short-term, subchronic, and chronic noncancer Health Based Values (HBVs) of 200, 30, and 5 µg/L, respectively. These HBVs were adopted as HRLs in 2009. In 2016, MDH re-evaluated the non-cancer HRLs, resulting in new noncancer short-term, subchronic, and chronic noncancer HBVs of 100, 60, and 9 µg/L, respectively. The short-term value was lower and the subchronic and chronic values were higher than previous guidance 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 into rule 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?	No	No	Yes	Yes	No
Effects observed?	¹	No	No ²	No ³	⁴

Comments on extent of testing or effects:

¹ Alachlor was not specifically tested for endocrine effects. Alachlor has been shown to cause an increase in thyroid weights at doses 2-fold higher than the subchronic and chronic critical study LOAEL. Thyroid tumors were also observed in rats exposed to doses ~6-fold higher than the subchronic and chronic critical study LOAEL.

² Developmental studies have reported increased resorptions and decreased litter size at dose levels ~13-fold higher than the short-term critical study LOAEL and ~50-fold higher than the

subchronic and chronic critical study LOAEL. The 3-generation study reported renal effects in rat pups at levels ~4-fold higher than the subchronic and chronic critical study LOAEL.

³ A single multigenerational study has been conducted. No effect on reproductive parameters was reported, however, significant decreases in ovarian weight were observed in the F0, parental generation. No microscopic changes were reported.

⁴ Based on toxicity profile for alachlor, OPP concluded that a developmental neurotoxicity study was not needed.

Resources Consulted During Review:

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World Health Organization (WHO). (2011). "Guidelines for Drinking Water Fourth Edition." from http://apps.who.int/iris/bitstream/10665/44584/1/9789241548151_eng.pdf.