



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

Chemical Name: Metolachlor and S-Metolachlor

CAS # : 51218-45-2 and 87392-12-9

Synonyms: *Dual; Pennant; Primagram; Primextra; Turbo*

Acute Non-Cancer Health Risk Limit (nHRL_{acute}) = 400 µg/L

$$\begin{aligned} &= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Acute intake rate, L/kg/d})} \\ &= \frac{(0.24 \text{ mg/kg/d}) \times (0.5) \times (1000 \text{ µg/mg})}{(0.289 \text{ L/kg-d})} \\ &= 415.2 \text{ rounded to } \mathbf{400 \text{ µg/L}} \end{aligned}$$

Reference Dose:	0.24 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	23.5 mg/kg-d (NOAEL, based on a 2 generation rat study by Smith et al, 1981 (Ciba-Geigy) as cited by EPA 1994 & 1995)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	100
UF allocation:	10 fold for interspecies extrapolation and 10 for intraspecies variability
Critical effect(s):	reduced pup weights
Co-critical effect(s):	None
Additivity endpoint(s):	Developmental (decreased body weight)
Secondary effect(s):	None

Short-term Non-Cancer Health Risk Limit (nHRL_{short-term}) = 400 µg/L

$$\begin{aligned} &= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Short-term intake rate, L/kg/d})} \\ &= \frac{(0.24 \text{ mg/kg/d}) \times (0.5) \times (1000 \text{ µg/mg})}{(0.289 \text{ L/kg-d})} \\ &= 415.2 \text{ rounded to } \mathbf{400 \text{ µg/L}} \end{aligned}$$

Reference Dose: 0.24 mg/kg-d (laboratory animal)
 Source of toxicity value: MDH, 2009
 Point of Departure: 23.5 mg/kg-d (NOAEL, based on a 2 generation rat study by Smith et al, 1981 (Ciba-Geigy) as cited by EPA 1994 & 1995)
 Human Equivalent Dose Adjustment: Insufficient data
 Total uncertainty factor: 100
 UF allocation: 10 fold for interspecies extrapolation and 10 for intraspecies variability
 Critical effect(s): reduced pup weights
 Co-critical effect(s): None
 Additivity endpoint(s): Developmental (decreased body weight)
 Secondary effect(s): None

Subchronic Non-Cancer Health Risk Limit (nHRL_{subchronic}) = 300 µg/L

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

$$= \frac{(0.097 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.077 \text{ L/kg-d})}$$

$$= 251.9 \text{ rounded to } \mathbf{300 \text{ µg/L}}$$

Reference Dose: 0.097 mg/kg-d (laboratory animal)
 Source of toxicity value: MDH, 2009
 Point of Departure: 9.7 mg/kg-d (NOAEL, based on a 1 year dog study, MRID 409807-01 as cited by EPA 1995 & 2002)
 Human Equivalent Dose Adjustment: Insufficient data
 Total uncertainty factor: 100
 UF allocation: 10 fold for interspecies extrapolation and 10 for intraspecies variability
 Critical effect(s): Decreased body weight in adult
 Co-critical effect(s): None
 Additivity endpoint(s): None (Body weight effects in adults are not utilized for additivity)
 Secondary effect(s): Decreased body weight in pups

Chronic Non-Cancer Health Risk Limit (nHRL_{chronic}) = nHRL_{subchronic} = 300 µg/L

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

$$= \frac{(0.097 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ } \mu\text{g/mg})}{(0.043 \text{ L/kg-d})}$$

$$= 451.2 \text{ rounded to } 500 \text{ } \mu\text{g/L}$$

Reference Dose: 0.097 mg/kg-d (laboratory animal)
Source of toxicity value: MDH, 2009
Point of Departure: 9.7-mg/kg-d (NOAEL, based on a 1 year dog study, MRID 409807-01 as cited by EPA 1995 & 2002)
Human Equivalent Dose Adjustment: Insufficient data
Total uncertainty factor: 100
UF allocation: 10 fold for interspecies extrapolation and 10 for intraspecies variability. (Based on comparison of effects observed after various durations of exposure the application of a subchronic-to-chronic UF was determined to be unnecessary)
Critical effect(s): Decreased body weight in adult
Co-critical effect(s): None
Additivity endpoint(s): None (Body weight effects in adults are not utilized for additivity)
Secondary effect(s): Decreased body weight in pups; increased liver weight

The Chronic nHRL must be protective of the subchronic exposures that occur within the chronic period and therefore, the Chronic nHRL is set equal to the Subchronic nHRL of 300 µg/L. Additivity Endpoints: None.

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification: Group C “possible human carcinogen” Nonlinear approach recommended (EPA 1995, 2002, 2006)
Slope factor: None
Source of slope factor: None
Tumor site(s): Liver

The chronic RfD (0.097 mg/kg-d) is protective for cancer risk.

Volatile: No

Summary of Guidance Value History:

The acute, short-term, and subchronic nHRLs are new values. The chronic nHRL (300 µg/L) is three times higher than the 1993/94 nHRL (100 µg/L), due to: 1) the removal of the group C factor, 2) more

recent intake rates which incorporate higher intake rates during early life, and 3) the value has been rounded to one significant digit.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No ¹	No	Yes	Yes	No ³
Effects?	--	--	Yes ²	Yes 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:

¹ Not tested. Increased relative thyroid weights were observed in F1 males in the multigenerational study. Related compound, acetochlor, causes thyroid effects.

² Decreased pup weight was observed at the acute/short-term critical study LOAEL and is the basis of the acute and short-term nHRLs. These dose levels were ~ 2-3-fold higher than the subchronic and chronic critical study LOAEL. Decreased pup body weight has been listed as a subchronic and chronic secondary endpoint. Reduction in the number of implantations and increased resorptions resulting in decreased litter size have also been reported, but at dose levels greater than 30-fold higher than the acute/short-term, subchronic and chronic critical study NOAELs.

³ Not tested. Related compound, acetochlor, causes neurological effects.

References:

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<http://www.who.int/ipcs/assessment/en/> (accessed 2/28/07); Background document for development of WHO Guideline for Drinking-Water quality
http://www.who.int/water_sanitation_health/dwq/chemicals/metolachlor.pdf (accessed 10/22/08)