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$_{\text{acute}}$) = 400 μg/L

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

Short-term Non-Cancer Health Risk Limit (nHRL$_{\text{short-term}}$) = 400 μg/L

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

\[
= (\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})
\]
\[
= \frac{(0.097 \text{ mg/kg/d}) \times (0.2) \times (1000 \mu g/mg)}{(0.077 \text{ L/kg-d})}
\]
\[
= 251.9 \text{ rounded to 300 µg/L}
\]

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
\[
\text{Chronic intake rate, L/kg/d} = (\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor}) \\
= (0.097 \text{ mg/kg/d}) \times (0.2) \times (1000 \mu g/mg) \\
= 451.2 \text{ rounded to } 500 \mu g/L
\]

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 \mu g/L. Additivity Endpoints: None.

Cancer Health Risk Limit (cHRL) = Not Applicable

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 \mu g/L) is three times higher than the 1993/94 nHRL (100 \mu g/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:

<table>
<thead>
<tr>
<th>Tested?</th>
<th>Endocrine</th>
<th>Immunotoxicity</th>
<th>Development</th>
<th>Reproductive</th>
<th>Neurotoxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No¹</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No³</td>
</tr>
</tbody>
</table>

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:


Environmental Protection Agency (EPA) 1991. Memorandum: Review additional discussion on Metolachlor’s carcinogenicity potential, a chronic dog study with additional data and additional metabolism data. Contains Data Evaluation Records (DERs) for Metolachlor metabolism in the Rat and Metolachlor 13/52-Week Oral Toxicity Study in Dogs.


EPA 1995 Metolachlor Reregistration Eligibility Decision

EPA Drinking Water Standards and Health Advisories (2000)


EPA 2006. S-metolachlor. Human Health Risk Assessment for Proposed Section 18 Uses on Cilantro, Collards, Kale, and Mustard Greens; Section 3 use on Pumpkin and Tolerance on Winter Squash without US Registration. PC Code 108800 S-metholachlor & 108801 Metolachlor. (7/13/06)

EPA Region 3 RBC table: (10/02) http://www.epa.gov/reg3hwmd/risk/human/index.htm (accessed 2/28/07)

EPA Region 9 PRG table: (10/02) http://www.epa.gov/region09/waste/sfund/prg/index.html (accessed 2/28/07)


Health Effects Assessment Summary Tables (HEAST): Table 1-information from IRIS-(07/1991), (accessed 2/28/07)

New York State Human Health Fact Sheet for Metolachlor, 2003. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Personal communication from Dr. Kenneth Bogdan, New York State Department of Health.


World Health Organization:(1993)
http://www.who.int/water_sanitation_health/dwg/chemicals/metolachlor.pdf (accessed 10/22/08)