2013 Health-Based Guidance for Water
Health Risk Assessment Unit, Environmental Health Division
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Toxicological Summary for Chlorpyrifos:

CAS**: 2921-88-2**
Synonyms: Lorsban, Govern, Pilot, Dursban, Empire, Brodan, Detmol UA, Dowco 179, Eradex, Paqeant

Acute Non-Cancer Health Based Value ($nHBV_{Acute}$) = 2 ug/L

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

$$= \frac{\text{(0.0036 mg/kg/d) x (0.2)* x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 2.49 rounded to **2 ug/L**

* MDH utilizes the EPA Exposure Decision Tree (EPA 2000) to select appropriate Relative Source Contributions (RSCs) (MDH 2008, Appendix K). Typically an RSC of 0.5 is utilized for moderately volatile contaminants for the acute and short-term durations. Given the high potential for exposure from other sources, an RSC of 0.2 was selected rather than applying the default RSC value of 0.5.

Reference Dose/Concentration:	0.0036 mg/kg-d (CD(SD) rats)
Source of toxicity value:	MDH, 2013
Point of Departure (POD):	0.36 mg/kg-d ($BMDL_{10}$, MRID 48139301, EPA, 2011 and Marty et al. 2012)
Human Equivalent Dose (MDH, 2011):	Not applied
Total uncertainty factor:	100
Uncertainty factor allocation:	10 for interspecies extrapolation (toxicokinetics and toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Inhibition of erythrocyte acetylcholinesterase
Co-critical effect(s):	None
Additivity endpoint(s):	Nervous system

Short-term Non-Cancer Health Based Value ($nHBV_{Short\text{-}term}$) = 0.6 ug/L

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

$$= \frac{\text{(0.0009 mg/kg/d) x (0.2)* x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 0.62 rounded to **0.6 ug/L**

*Rationale for selecting an RSC of 0.2 - same explanation as that provided for the acute duration (see above).

Reference Dose/Concentration:	0.0009 mg/kg-d (CD(SD) rats)
Source of toxicity value:	MDH, 2013

Point of Departure (POD):	0.09 mg/kg-d ($BMDL_{10}$, MRID 48139301, EPA, 2011 and Marty et al. 2012)
Human Equivalent Dose (MDH, 2011):	Not applied
Total uncertainty factor:	100
Uncertainty factor allocation:	10 for interspecies extrapolation (toxicokinetics and toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Inhibition of erythrocyte acetylcholinesterase
Co-critical effect(s):	None
Additivity endpoint(s):	Nervous system

Subchronic Non-Cancer Health Based Value ($nHBV_{Subchronic}$) = $nHBV_{Short\text{-}term}$ = 0.6 ug/L

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

$$= \frac{\text{(0.00023 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)*}}$$

= 1.1 rounded to 1 ug/L

*RfD is based on sensitivity to cholinesterase inhibition during pregnancy therefore the intake rate for pregnant women is utilized rather than the default child (0-8 years of age) intake rate (see SONAR MDH, 2008, page 43).

Reference Dose/Concentration:	0.00023 mg/kg-d (SD rats)
Source of toxicity value:	MDH, 2013
Point of Departure (POD):	0.03 mg/kg-d ($BMDL_{10}$, Mattsson et al., 1998/MRID 44556901, aci EPA, 2011)
Human Equivalent Dose (MDH, 2011):	0.03 mg/kg-d x 0.23 = 0.0069 mg/kg-d
Total uncertainty factor:	30
Uncertainty factor allocation:	3 for interspecies extrapolation (to address potential differences in toxicodynamics); 10 for intraspecies variability
Critical effect(s):	Inhibition of erythrocyte acetylcholinesterase
Co-critical effect(s):	None
Additivity endpoint(s):	Nervous system

The Subchronic nHBV must be protective of the acute and short-term exposures that occur within the subchronic period and therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 0.6 ug/L. Additivity Endpoints: Nervous system

Chronic Non-Cancer Health Based Value ($nHBV_{Chronic}$) = $nHBV_{Short\text{-}term}$ = 0.6 ug/L

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

$$= \frac{\text{(0.00023 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 1.1 rounded to 1 ug/L

Reference Dose/Concentration: Same as Subchronic RfD, see information above for details about the reference dose.

The Chronic nHBV must be protective of the acute and short-term exposures that occur within the chronic exposure period and therefore, the Chronic nHBV is set equal to the Short-term nHBV of 0.6 ug/L. Additivity Endpoints: Nervous system

Cancer Health Based Value (cHBV) = Not Derived/Not Applicable

Volatile: Yes (moderate)

Summary of Guidance Value History: MDH previously developed an HBV in 1995 for chlorpyrifos of 20 ug/L. The short-term, subchronic and chronic HBVs presented above (0.6 ug/L) are approximately 30-fold lower as the result of: 1) more recent toxicological information resulting in a lower RfD; 2) use of more recent water intake rates which incorporate higher intake rates during early life; 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?	Yes	Yes	Yes	Yes	Yes
Effects?	Yes[1]	Yes[2]	Yes[3]	Yes[4]	Yes[5]

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]Endocrine effects following oral exposure to chlorpyrifos have been reported after very high doses 500-10,000 times higher than the RfD. Sheep thyroid hormone levels decreased after repeated administration of chlorpyrifos at levels more than 10,000 times higher than the short-term RfD. Pregnant rodents given chlorpyrifos slightly decreased circulating thyroid hormone levels at more than 3,000 times higher than the short-term RfD.

[2]Immunotoxicity in the form of alterations in the number of T-regulatory cells in the spleen and a reduced immune response in rodents exposed *in utero* and through early life has been reported at a dose more than 10,000 times higher than the short-term RfD.

[3]Developmental effects following chlorpyrifos exposure have been observed only at high doses more than 1,000 times greater than the short-term RfD. These effects include increased pup mortality, brain structure alterations, and other less severe effects in rodents. A rabbit study demonstrated slight decreases in fetal weight and crown to rump lengths at a dose over 70,000 times higher than the short-term RfD. Neurodevelopmental effects are also noted below in footnote 5.

[4]Reproductive effects were noted in one rat study as an increase in post-implantation loss in animals exposed to doses more than 10,000 times higher than the short-term RfD.

[5]The critical effect following chlorpyrifos exposure is neurotoxicity, through inhibition of the nervous system

enzyme acetylcholinesterase. Pregnancy results in the loss of certain enzymes that detoxify chlorpyrifos, and is associated with increased sensitivity to acetylcholinesterase inhibition. Other neurological effects have been noted at higher doses, such as changes in brain cells and brain structures and alterations in behavioral tests in rodents. These effects occurred at doses greater than 250 times higher than the RfD established for chlorpyrifos. Very slight but statistically significant neurodevelopmental effects were noted in the parietal cortex at approximately 250 times higher than the RfD.

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