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

CAS**: 5598-15-2**
Synonyms: Chlorpyrifos oxygen analog, Lorsban oxygen analog, Dursbanoxon, 3,5,6-Trichloro-2-pyridyl diethyl phosphate

**Acute Non-Cancer Risk Assessment Advice ($nRAA_{Acute}$) = 0.9 ug/L**

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

$$= \frac{\text{(0.0005 mg/kg/d) x (0.5) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 0.87 rounded to **0.9 ug/L**

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| Reference Dose/Concentration: | 0.0005 mg/kg-d (CD(SD) rats) |
| Source of toxicity value: | MDH, 2013 |
| Point of Departure (POD): | 0.05 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 Risk Assessment Advice ($nRAA_{Short\text{-}term}$) = 0.4 ug/L**

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

$$= \frac{\text{(0.00008 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)*}}$$

= 0.37 rounded to **0.4 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 infant intake rate (see SONAR, MDH, 2008, page 43). Since the short-term duration intake is based on pregnant women, not infants, an RSC of 0.2 is utilized. Based on available information, the Short-term nRAA is protective of developmental effects.

Reference Dose/Concentration: 0.00008 mg/kg-d (CD(SD) rats)

| | |
|---|---|
| Reference Dose/Concentration: | 0.00008 mg/kg-d (CD(SD) rats) |
| Source of toxicity value: | MDH, 2013 |
| Point of Departure (POD): | 0.024 mg/kg-d ($BMDL_{10}$, MRID 48139301, EPA, 2011 and Marty et al. 2012) |
| Human Equivalent Dose (MDH, 2011): | Not applied |
| Total uncertainty factor: | 300 |
| Uncertainty factor allocation: | 10 for interspecies extrapolation (toxicokinetics and toxicodynamics), 10 for intraspecies variability, 3 for database uncertainty (pregnant rats demonstrated a 3-fold higher sensitivity to chlorpyrifos exposure however studies are lacking for the oxon) |
| Critical effect(s): | Inhibition of erythrocyte acetylcholinesterase |
| Co-critical effect(s): | None |
| Additivity endpoint(s): | Nervous system |

**Subchronic Non-Cancer Risk Assessment Advice ($nRAA_{Subchronic}$) = $nRAA_{Short-term}$ = 0.4 ug/L**

**Chronic Non-Cancer Risk Assessment Advice ($nRAA_{Chronic}$) = $nRAA_{Short-term}$ = 0.4 ug/L**

**The Subchronic and Chronic duration nRAAs must be protective of shorter duration exposures that occur within the subchronic and chronic periods and therefore the Short-term nRAA based on protecting pregnant women is applied.**

Note: No oral subchronic or chronic chlorpyrifos oxon studies have been conducted. The $nRAA_{Short-term}$ is used without additional uncertaintly factors because it has been demonstrated that the toxicity of chlorpyrifos and other acetylcholinesterase inhibitors does not increase as duration of exposure increases from short-term to chronic. In addition, existing longer duration oral chlorpyrifos studies can be used to support the basis for not applying an uncertainty factor to subchronic and chronic chlorpyrifos oxon exposures as these two chemicals share the same mechanism of action.

**Cancer Risk Assessment Advice (cRAA) = Not Applicable**

**Volatile: Yes (moderate)**

**Summary of Guidance Value History:** Chlorpyrifos-oxon has no previous MDH guidance.

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

| | Endocrine | Immunotoxicity | Development | Reproductive | Neurotoxicity |
|---|---|---|---|---|---|
| Tested? | No[1] | No[1] | No[1] | No[1] | Yes |
| Effects? | -- | -- | -- | -- | 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]No oral endocrine, immunotoxicity, developmental, or reproductive studies have been conducted with chlorpyrifos-oxon. As chlorpyrifos oxon and its parent compound are similar toxicologically, see the chlorpyrifos Health Standards Statute table for further information regarding potential endocrine, immune, developmental, and reproductive effects possible at high doses of chlorpyrifos oxon.

[2]Neurotoxicity through inhibition of acetylcholinesterase is the established critical effect of chlorpyrifos oxon exposure and forms the basis of the short-term RfD. Other neurotoxic effects have been reported, but only at doses >1,000 times the short-term RfD for chlorpyrifos oxon.

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