# Chlorpyrifos

| CAS number: | 2921-88-2 |
| --- | --- |
| Synonyms: | O,O-diethyl O-(3,5,6-trichloro-2-pyrindinyl) phosphorothioate, brodan, dowco 179, dursban,  ENT-27,311, eradex, lorsban, chlorpyriphos |
| Chemical formula: | C9H11Cl3NO3PS |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | 0.1 mg/m3 (0.007 ppm) |
| --- | --- |
| STEL: | — |
| Peak limitation: | — |
| Notations: | Sk. |
| IDLH: | — |
| **Sampling and analysis**: The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 0.1 mg/m3 is recommended to protect for cholinesterase (ChE) inhibition in exposed workers.

## Discussion and conclusions

Chlorpyrifos is a broad-spectrum organophosphate pesticide used widely on plants, animals, some building structures and household pests (ACGIH 2003; HCOTN 2003).

Based on human and animal data, the critical effect of exposure is ChE inhibition. Occupational exposures at 0.4 mg/m3 are reported to be without adverse effect. In animals, NOAEL range depending on whether the endpoint is brain, plasma or serum ChE activity (HCOTN, 2003). A critical inhalation study reported no effects on ChE activity in rats exposed at 0.3 mg/m3 for six hours per day for 13 weeks. An oral NOEL of 0.1 mg/kg for ChE inhibition endpoints in multiple animal species. This dose corresponds to an inhalation concentration of 0.7 mg/m3 based on generic exposure factors (ACGIH, 2018).

On a weight of evidence, a TWA of 0.1 mg/m3 is recommended to limit the symptoms associated with the critical effect.

## Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

A skin notation is recommended due to the potential for significant dermal absorption as reported in animal studies.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 0.2 mg/m3 | |
|  |
| ACGIH 2003 TLV-TWA: 0.1 mg/m3 (inhalable aerosol and vapor) |
| TLV-TWA recommended to minimise cholinergic symptoms and other harmful biological effects in exposed workers.  Inadequate data to recommend SEN Notation or a TLV-STEL. A Skin notation is assigned.  Summary of data:  Human data:   * Extensively distributed upon absorption; blood half-life ≈27 h   + metabolites reported in urine of pesticide workers as indirect evidence of inhalation absorption * Case studies of ingestion:   + 300 mg/kg: unconsciousness, cyanosis, wheezing, uncontrollable urination, diarrhoea within 18 h; plasma ChE almost 0 at 36 h and RBC ChE activity 60% at 30 d   + unknown amount (assumed to be a high concentration): extreme agitation, muscle weakness and contractions at 14 h; RBC ChE activity within normal limits * Immediate and delayed toxicity effects reported in workers including:   + immediate effects of nausea, headaches, vomiting, light headedness and muscle cramps   + delayed effects of paraesthesia in feet, groin, suprapubic and thigh pain, memory impairment, distal axonopathy, numbness of legs   + many effects resolve within 2 wk to 3 mo after cessation of exposure * 0.01-0.37 mg/m3 associated withno statistically significant differences in illness or prevalence of symptoms and no indication of RBC ChE inhibition   + update of study reported exposed workers reported symptoms more often than comparison group including dizziness, malaise and fatigue; no relation with exposure identified * ≥0.1 mg/kg/d reported no RBC ChE inhibition (n=16 volunteers)   + mean plasma ChE activity inhibited at 0.1 mg/kg/d compared to control * 5 mg/kg dermally reported no signs of RBC ChE inhibition (n=6 male volunteers)   + plasma ChE activity reduced to 15% of pre-dose levels after oral exposure of 0.5 mg/kg. * US EPA concluded that reports of birth defects following *in utero* exposure were insufficient evidence of teratogenicity.   Animal data:   * Toxic symptoms reported in animals include neurotoxicity, hypoactivity, lacrimation, salivation, foot splay, ataxia, tremors * LD50: 80–250 mg/kg/d range (mammals, oral) * LD50: 202 mg/kg (male rats, dermal) * Calculated inhalational lethal dose: 78 and 94 mg/kg (female mice and rats, respectively) based on 60-180 min exposures * Tolerance to prolonged and significant AChE inhibition reported in rats (subcutaneous injection) * NOAEL of 0.1 mg/kg/d for ChE inhibition endpoints in multiple species (oral; monkeys, dogs, rats) * No RBC ChE inhibition in rats at 0.3 mg/m3 for 6 h/d, 5 d/wk for 13 wk (inhalation) * No signs of toxicity or carcinogenicity observed in exposed rats and dogs to exposure of up to 3 mg/kg for 2 or 3 yr * Decreased pup body weight and increased mortality in F1 litters following parental toxicity in rats at 5 mg/kg/d   + cellular defects (reduced cell size) in developing brain of pups after 1 or 5 mg/kg/d exposure also reported.   Genotoxicity:   * Induced micronuclei in erythroblasts and caused cytogenetic effects in human lymphoid cells (dose-related) * Produced significant increases in SCE, X chromosome loss and sex-linked recessive lethality in *Drosophila melanogaster*.   TLV-TWA justification:   * Repeat dose of 0.1 mg/kg in animals considered to be NOEL * Assuming 70 kg worker inhales 10 m3 air/8 h shift and 100% absorption ≡0.7 mg/m3 * Supported by studies in workers report ≈0.4 mg/m3 and rats ≈0.3 mg/m3 without effects. |
| DFG 2008 Not assigned |
| No additional information. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2003 TWA: 0.2 mg/m3 |
| TWA recommended to protect against inhibition of AChE activity in brain tissue as critical effect.  Skin notation is recommended.  Summary of additional data:   * 72% of inhaled vapours absorbed (calculated from nose-only study in F344 rats) * 2% dermal absorption in 120 h; 74% in mice in 8 h * Case study of ingestion:   + unknown amount (assumed to be a high concentration): stupor, respiratory distress, complete inhibition serum ChE activity; undetectable serum ChE activity after 1 mo   + unknown amount (assumed to be a high concentration): pupillary constriction, excess secretions, tachycardia, impaired consciousness * 6 mo worker exposure in closed environment: lachrymation, muscle twitching, RBC AChE inhibition, paraesthesia and numbness, sensory loss, weakness, decreased reflexes in legs; remission in 1 yr (no further information about concentration) * Higher rate of atopy, antibiotic sensitivities, elevated CD26 cells (activated T cells) and autoimmunity reported in exposed group compared to control group * Various NOAEL reported in animals; lowest being 0.01 mg/m3 for plasma ChE inhibition, >0.287 mg/m3 (rats, inhalational) for brain AChE inhibition and 1 mg/kg (body weight; acute oral) for RBC AChE inhibition   Mutagenicity and genotoxicity:   * Negative for induction of mitotic recombination in *S. cerevisiae* and increase in unscheduled DNA synthesis *in vitro* * Induced clastogenic and DNA-damaging effects in some *in vivo* tests. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| US EPA |  | 1987 | * Oral RfD withdrawn in 2011 * Inhalation RfC not evaluated * Carcinogenic assessment not evaluated for evidence of human carcinogenic potential. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | No |
| --- | --- |
| **The chemical is not a non-threshold based genotoxic carcinogen.** |  |

## Notations

| Source | Notations |
| --- | --- |
| SWA | NA |
| HCIS | NA |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | Carcinogenicity – A4, Skin |
| DFG | NA |
| SCOEL | NA |
| HCOTN | Skin |
| IARC | NA |
| US NIOSH | NA |

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

### Skin notation assessment

| Calculation |
| --- |
| |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Conclusion:** |  |  |  |  |  |  |  |  |  | |  |  | Adverse effects in human case study: | yes | 4.00 |  |  |  |  |  | |  |  | Dermal LD50 ≤1000 mg/kg: | yes |  |  |  |  |  |  | |  |  | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  |  |  |  |  | |  |  | Dermal LD50/Inhalation LD50 <10: |  |  |  |  |  |  |  | |  |  | *In vivo* dermal absorption rate >10%: |  |  |  |  |  |  |  | |  |  | Estimated dermal exposure at WES >10%: |  |  |  |  |  |  |  | |  |  |  |  |  | **a skin notation is warranted** | | | |  | |

### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

| Molecular weight: | 350.59 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 14.34 mg/m3; 1 mg/m3 = 0.06974 ppm |
| This chemical is used as a pesticide: |  |
| This chemical is a biological product: |  |
| This chemical is a by-product of a process: |  |
| A biological exposure index has been recommended by these agencies: | ACGIH  DFG  SCOEL |

## Workplace exposure standard history

| Year | Standard |
| --- | --- |
| 1991 | 0.2 mg/m3 |

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [*TLVs® and BEIs® Guidelines section*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2008) Organophosphates – The MAK-Collection Part IV: Biomonitoring Methods, Vol. 11.

Health Council of the Netherlands (HCOTN) (2003) Chlorpyrifos. Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/067.

U.S. Environmental Protection Agency (US EPA). (1987). Chemical Assessment Summary – Chlorpyrifos; CASRN 2921-88-2. Integrated Risk Information System (IRIS).