

# METHYL PARATHION

**CAS number:** 298-00-0

**Synonyms:** Azophos, Bladan M, O,O-dimethyl O-(p-nitrophenyl) phosphorothioate, Metron, Nitrox, Dalf, Foidol-M, Metacide

**Chemical formula:**  $C_8H_{10}NO_5PS$

## Workplace exposure standard (amended)

**TWA:** 0.02 mg/m<sup>3</sup>

**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 0.02 mg/m<sup>3</sup> is recommended to protect for cholinergic effects in exposed workers.

## Discussion and conclusions

Methyl parathion is used as a broad-spectrum insecticide.

The critical effect of exposure is cholinesterase (ChE) inhibition, which leads to typical cholinergic symptoms at high concentrations including headaches, nausea, psychosis, paralysis, convulsions and coma (ACGIH, 2018). Inhalational exposure data are limited, but several well-documented oral dose studies exist. A NOAEL of 0.3 mg/kg/day and LOAEL of 0.4 mg/kg/day for red blood cell (RBC) ChE inhibition without clinical cholinergic symptoms in volunteers are reported. These effect levels in humans are consistent with those determined in subchronic and chronic animal feeding studies, which report NOAEL between 0.1 and 0.3 mg/kg/day and LOAEL between 1 and 3 mg/kg/day. The dose-response relationship is steep with increased mortality reported at 2.5 mg/kg/day in one study (ACGIH, 2018).

In the absence of suitable inhalational exposure data, the recommended TWA is based on the oral NOAEL of 0.3 mg/kg/day in humans and is supported by the results of subchronic and chronic animal feeding studies. Applying generic conversion factors, a corresponding NOAEC is approximately 0.04 mg/m<sup>3</sup>. The TWA of 0.02 mg/m<sup>3</sup> derived by ACGIH (2018) is recommended to be adopted, and presumably based on the NOAEL of 0.3 mg/kg/day in humans divided by an uncertainty factor of two. This TWA is expected to be protective of ChE inhibition.

## 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 based on evidence for dermal absorption and adverse systemic effects in animals.

DRAFT

## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>1991</b>	<b>TWA: 0.2 mg/m<sup>3</sup></b>
<b>ACGIH</b>	<b>2009</b>	<b>TLV-TWA: 0.02 mg/m<sup>3</sup></b>
<p>TLV-TWA intended to protect for RBC ChE inhibition and cholinergic nervous system effects at higher concentrations.</p> <p>Equivocal results from mutagenicity assays and not classifiable as a human carcinogen based on negative results in chronic animal feeding studies.</p> <p>Skin notation is warranted based on dermal application studies with rabbits.</p> <p>Summary of data:</p> <p>TLV-TWA based on several oral dose studies in humans and animals. A NOAEL of 0.3 mg/kg/d for ChE inhibition is determined in humans, supported by NOAELs of 0.1 mg/kg/d in rats with corresponding LOAELs of 0.5 mg/kg/d in both subchronic and chronic feeding studies.</p> <p>Target organ is the liver; excretion occurs <i>via</i> urine.</p> <p>TLV-TWA derivation not discussed.</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>Cholinergic symptoms occur within minutes of toxic exposures and may last several days; <ul style="list-style-type: none"> <li>no evidence for delayed neuropathy in available data</li> </ul> </li> <li>Effects of poisoning occur at 1–31% RBC ChE inhibition <ul style="list-style-type: none"> <li>headache, malaise, insomnia and anorexia in exposed worker with 13% RBC ChE inhibition</li> </ul> </li> <li>No cholinergic effects or ChE inhibition at 0.03 and 0.06 mg/kg/d in volunteer oral dose study (n=2, 5 d)</li> <li>NOAEL: 0.3 mg/kg/d for ChE inhibition in volunteer oral dose study (n=5, 30 d) <ul style="list-style-type: none"> <li>55% RBC cholinesterase inhibition, but no clinical signs of cholinergic toxicity at 0.4 mg/kg/d reported in 1/5 volunteers.</li> </ul> </li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>LD<sub>50</sub>: 67 mg/kg (rats, dermal)</li> <li>LD<sub>50</sub>: 14–24 mg/kg (rats, oral)</li> <li>LC<sub>50</sub>: 200 mg/m<sup>3</sup> (rats, 1 h), 120 mg/m<sup>3</sup> (rats, 4 h)</li> <li>Detoxification in the liver was blocked by pre-treatment with chlorpyrifos (rats)</li> <li>Habituation observed in repeat subcutaneous injection study at 3 mg/kg (rats, &gt;9 doses)</li> <li>No change to immune function parameters at 0.2–0.9 mg/kg/d in repeat oral dose study (rats, 28 d); increased liver weights at &gt;0.4 mg/kg/d</li> <li>Several subchronic and chronic feeding studies report NOAELs of 0.1 mg/kg/d for ChE inhibition with corresponding LOAELs 1–3 mg/kg/d (rats, 90 d or 2 yr); <ul style="list-style-type: none"> <li>similar results obtained in dogs with NOAEL: 0.3 mg/kg/d and LOAEL: 0.7 mg/kg/d; cholinergic effects, haematological changes and mortality at 2.5 mg/kg/d</li> <li>no adverse effects, but ChE inhibition reported at 0.03–3 mg/kg/d in another study (dogs, 2 yr)</li> <li>no carcinogenic activity reported in any chronic feeding studies up to 50 mg/kg/d</li> </ul> </li> <li>RBC ChE inhibition at 10 and 100 mg/kg in repeat dermal dose study (rabbits, 21 d)</li> </ul>		

Source	Year set	Standard
		<ul style="list-style-type: none"> <li>no effects noted at 1.5 mg/kg</li> <li>Cholinergic effects, RBC and brain ChE inhibition and severe liver/kidney damage at 2 mg/kg/d in repeat dermal dose study (rats, 30 d); effects at 1.5 mg/kg/d (rabbits)</li> <li>Results of several mutagenicity assays are equivocal; <ul style="list-style-type: none"> <li>positive and negative results <i>in vitro</i> in bacterial systems with or without metabolic activation</li> <li>negative results for dominant lethal mutations at 10–60 ppm in diet or 0.03 mg/kg/d in drinking water (mice, 7 wk)</li> </ul> </li> <li>Foetal malformations observed at 60 mg/kg/d (rats, GD 6–15); <ul style="list-style-type: none"> <li>no foetal toxicity at maternally non-toxic doses in several developmental studies</li> </ul> </li> <li>No evidence for long-term accumulation from single oral dose at 3 mg/kg/d (rats), substance detected in adipose tissue and liver, respective organ half-lives: 15 and 13 d.</li> </ul> <p>Insufficient data to assign a TLV-STEL or sensitisation notation.</p>
<b>DFG</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>SCOEL</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>OARS/AIHA</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>HCOTN</b>	<b>NA</b>	<b>NA</b>
No report.		

## Secondary source reports relied upon

Source	Year	Additional information
NICNAS	* 2018	Tier I: agricultural uses not assessed.
IARC	✓ 1983	<ul style="list-style-type: none"> <li>Insufficient evidence for carcinogenic activity in experimental animals; no data available for humans</li> <li>No evidence for a carcinogenic risk to humans in available database.</li> </ul>
US EPA	✓ 1987	<ul style="list-style-type: none"> <li>NOAEL: 0.025 mg/kg/d for ChE inhibition and haematological changes with LOAEL: 0.25 mg/kg/d in chronic feeding study (rats, 2 yr, also cited in ACGIH, 2018) used principally to derive oral RfD</li> <li>Inhalation RfD and carcinogenicity not yet evaluated.</li> </ul>
US NIOSH	✓ 2015	<ul style="list-style-type: none"> <li>No ChE inhibition reported in wine growers exposed by dermal contact and inhalation to 0.002–12 mg and 0.022 mg, respectively (n=23, 50 min)</li> <li>Calculated 24–48 h dermal absorption: 5.20–8.99% in acetone or 1.35–3.58% as commercial formulation</li> <li>Positive dermal sensitisation reported in 1/294 volunteers insufficient to classify as dermal sensitiser</li> </ul>



Source	Year	Additional information
		<ul style="list-style-type: none"> <li>NOAEL: 0.1 mg/kg/d for ChE inhibition and memory/motor function impairment with LOAEL of 1 mg/kg/d in repeat dermal application study (rabbits, 28 d).</li> </ul>

## Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Insufficient data

Is the chemical carcinogenic with a mutagenic mechanism of action? No

**The chemical is not a non-threshold based genotoxic carcinogen.**

## Notations

Source	Notations
SWA	Skin
HCIS	—
NICNAS	NA
EU Annex	NA
ECHA	—
ACGIH	Carcinogenicity – A4, Skin
DFG	NA
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
US NIOSH	SK:SYS

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		
Adverse effects in human case study:	yes	
Dermal LD <sub>50</sub> ≤ 1000 mg/kg:	yes	
Dermal repeat-dose NOAEL ≤ 200 mg/kg:	yes	
Dermal LD <sub>50</sub> /Inhalation LD <sub>50</sub> < 10:	yes	
<i>In vivo</i> dermal absorption rate > 10%:	no	
Estimated dermal exposure at WES > 10%:		
<b>a skin notation is warranted</b>		

## IDLH

Is there a suitable IDLH value available? No

## Additional information

Molecular weight:	291.30
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 10.8 mg/m <sup>3</sup> ; 1 mg/m <sup>3</sup> = 0.09 ppm
This chemical is used as a pesticide:	<input checked="" type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input checked="" type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> SCOEL

## Workplace exposure standard history

Year	Standard
Click here to enter year	

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7<sup>th</sup> Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [TLVs® and BEIs® Guidelines section](#) on the ACGIH website.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

International Agency for Research on Cancer (IARC) Miscellaneous pesticides. IARC Monographs – volume 30.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) Phosphorothioic acid, O,O-dimethyl O-(4-nitrophenyl) ester: Human health tier I assessment – IMAP report.

US Environmental Protection Authority (US EPA) (1987) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Methyl parathion.

US National Institute for Occupational Safety and Health (NIOSH) (2015) NIOSH Skin Notation Profiles: Methyl Parathion.