# Mevinphos

| CAS number: | 7786-34-7 |
| --- | --- |
| Synonyms: | 2-Carboxymethoxy-1-methylvinyl dimethyl phosphate, crotonic acid 3-hydroxy- methyl ester dimethyl phosphate, O,O-dimethyl 1-carbomethoxy-1-propen-2-yl phosphate, 3-hydroxycrotonic acid methyl ester dimethyl phosphate, Menite, Mevinox, OS-2046, Phosfene |
| Chemical formula: | C7H13O6P |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **0.01 mg/m3** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Sk.** |
| IDLH: | **4 ppm** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 0.01 mg/m3 is recommended to protect for cholinergic effects in exposed workers.

## Discussion and conclusions

Mevinphos is an organophosphate that was widely used as an insecticide for flowers and crops. It is a restricted chemical that is still used for specific applications in Australia.

The critical effect of exposure is cholinesterase inhibition, which can cause reversible cholinergic neuromuscular stimulation.

Inhalational exposure data are limited, but several human and animal oral dose studies are available. A LOAEL of 0.015 mg/kg for red blood cell (RBC) cholinesterase inhibition without clinical cholinergic symptoms is reported in orally dosed volunteers. Doses between 0.02 to 0.04 mg/kg did not elicit cholinergic effects, but did increase RBC cholinesterase inhibition (ACGIH, 2018 and DFG, 2002). Comparable endpoints are presented in animals with NOAELs of 0.025 and 0.4 mg/kg in dogs and rats, respectively (ACGIH, 2018). Extrapolation of oral doses to inhalational exposure is complicated by first-pass detoxification evidenced in animals (DFG, 2002). As per the derivation presented by ACGIH (2018), conversion of the oral LOAEL in humans to an equivalent inhalational dose would yield an inhalational LOAEC of 0.1 mg/m3. A recommended TWA of 0.01 mg/m3 is derived by applying a factor of 10 to this LOAEC to account for the absence of an experimentally determined NOAEC and differences in detoxification pathways.

The recommended TWA is considered sufficiently low to be protective of short term exposures, therefore a STEL is not recommended.

## 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 warranted as evidence indicates rapid absorption through the skin and reports of acute poisonings in the workplace.

# Appendix

### Primary sources with reports

| Source Year set Standard | |
| --- | --- |
| SWA 1991 TWA: 0.01 ppm (0.092 mg/m3); STEL: 0.03 (0.27 mg/m3) |
|  |
| ACGIH 2003 TLV-TWA: 0.01 mg/m3 |
| TLV-TWA intended to protect for cholinesterase inhibition. Not classifiable as a human carcinogen based on negative results in chronic animal studies. A skin notation is recommended based on systemic toxicity observed in animals following dermal application.  Summary of data:  TLV-TWA derived from an oral dose LOAEL of 0.01 mg/kg for RBC inhibition without cholinergic effects in humans and supported by the same endpoint in animals at a NOAEL of 0.025 mg/kg/d. The human LOAEL is converted to an inhalational dose of 0.1 mg/m3 assuming a 70 kg worker with a respiratory volume of 10 m3 during an 8 h shift; a TLV-TWA of 0.01 mg/m3 is therefore considered protective.  Human data:   * Occupational exposure of 2 workers at 0.1 mg/kg from spray applications caused severe reduction in RBC cholinesterase activity, weakness, fasciculation and blurred vision * Several cases of poisoning following dermal contact from contaminated clothing * No cholinergic effects reported in any volunteers of repeat oral dose study (n=5, 30 d):   + LOAEL: 0.015 mg/kg/d for 17% RBC cholinesterase inhibition in 2/5 volunteers   + 0.04 mg/kg/d (highest tested dose) caused 17–34% inhibition in 5/5 volunteers   + similar results in related study (n=8, 28 d); 19% RBC and 13% plasma cholinesterase inhibition at 0.025 mg/kg/d without cholinergic effects, but decreased nerve conduction velocity and reflex force reported.   Animal data:   * Oral LD50: 3.4–6.1 mg/kg (rats), ip LD50: 1.5 mg/kg (rats); difference suggests first-pass liver detoxification; inhalational doses therefore expected to be more toxic than oral doses * Dermal LD50: 4.2–4.7 mg/kg (rats), 33.8 mg/kg (rabbits) * LC50: 9.8 mg/m3 and 73.6–92 mg/m3 (rats, 1 h) * No cumulative effects in repeat IP injection study at 10–50% LD50 (rats, 5 d/wk, 17–22 d) * 94% of oral dose and 16.8% of dermal dose absorbed (rats); oral dose excreted in urine (18%) and exhaled air (76%) * Sub-chronic feeding study (rats, 13–18 wk) with treatment range 0.02–16 mg/kg/d and one group fed 12 mg/kg/d (5 wk), 24 mg/kg/d (2 wk), 32 mg/kg/d (6 wk) reported:   + NOAEL: 0.4 mg/kg/d RBC cholinesterase activity progressively reduced >2 mg/kg   + LOAEL: 2 mg/kg/d, for cholinergic effects (tremors, ataxia, increased respiration) * Sub-chronic feeding study with treatment range 0.0075–5 mg/kg/d (dogs, 14 wk):   + NOAEL: 0.025 mg/kg/d for RBC cholinesterase inhibition   + LOAEL: 1.88 mg/kg/d for cholinergic symptoms * Unpublished data from repeat oral dose studies (frequency/durations not specified) reported NOEL: 0.025 mg/kg for vomiting (dogs), NOEL: 0.05 mg/kg for nasal/oral discharges (rats) and diarrhea (rabbits), NOEL: 0.1 mg/kg for tremors (rats) * Unpublished chronic feeding studies showed comparable endpoints to sub-chronic feeding studies and no evidence of carcinogenic activity:   + NOAEL: 0.025 mg/kg/d for RBC cholinesterase inhibition (dogs, no further details)   + NOAEL: 0.025 mg/kg/d for plasma and brain cholinesterase inhibition (rats, 1 yr); LOAEL: 0.35 mg/kg/d; same NOAEL for 2 yr exposure * Mutagenic *in vitro* in bacteria and Chinese hamster ovary (CHO) cells; increased sister chromatid exchange reported in CHO cells, but not unscheduled DNA synthesis.   Insufficient data available to assign a TLV-STEL or sensitisation notation. |
| DFG 1961 MAK: 0.01 ppm (0.093 mg/m3) |
| Summary of additional information:  Previous (1972) MAK of 0.01 ppm retained based on volunteer oral intake study with a NOAEL of 0.015 mg/kg/d (also cited in ACGIH, 2018), which equates to an inhalational dose of 0.1 mg/m3 (0.01 ppm) following conversion (not discussed) and is equal to the current MAK.  Previous evaluation did not consider MAK a threshold limit for cholinergic toxicity due to the lack of inhalational exposure data. The MAK was therefore previously based on human and animal oral exposure data with a large uncertainty factor (not discussed). Skin notation warranted based on several cases of poisoning via dermal contact.  Human data:   * Of 911 cases of pesticide poisonings in workers, 29 due to Mevinphos, follow-up investigations of the poisoned workers do not indicate delayed adverse effects * Low RBC cholinesterase inhibition (not specified) in workers exposed at   0.013–0.029 mg/m3 (duration not specified) during hops production   * 1 case of moderate intoxication from occupational exposure (concentration/duration not specified) reported peak concentration of dimethyl phosphate metabolite in urine of 0.4 mg/L after 12 h and was eliminated within 50 h * LOAEL of 0.015 mg/kg/d for RBC cholinesterase inhibition from volunteer study (n=5, 30 d, also cited in ACGIH, 2018) considered a NOAEL; 0.02–0.03 mg/kg caused 20% RBC cholinesterase inhibition in all volunteers and is considered the LOAEL by the agency.   Animal data:   * Induction of liver microsomal enzymes reduced acute toxicity (mice, rats) * Non-specific liver and kidney degeneration in sub-chronic feeding study at 2 mg/kg/d (rats, 13 wk, also cited in ACGIH, 2018). |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2018 | * Tier I: agricultural uses not assessed. |
| US NIOSH |  | 2015 | * Skin permeation coefficient (kp): 0.0001 cm/h; water solubility (Sw): 600 mg/cm3 * Available toxicokinetic data indicate potential for dermal absorption and systemic availability at acutely/fatally toxic levels in animals causing cholinesterase inhibition. |

### 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 | — |
| ECHA | NA |
| ACGIH | Carcinogenicity – A4, Skin |
| DFG | H (skin) |
| SCOEL | NA |
| HCOTN | NA |
| IARC | NA |
| 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 | 4.00 |  | | Dermal LD50 ≤1000 mg/kg: | yes | 3.00 |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <10: | no | -3.00 |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: | yes | 2.00 |  | |  |  | 0.6666667 | **a skin notation is warranted** | |

### IDLH

| Is there a suitable IDLH value available? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 224.15 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 9.17 mg/m3; 1 mg/m3 = 0.11 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 |
| --- | --- |
| Click here to enter year |  |

## 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) (2002) Mevinphos (Phosdrin) – MAK value documentation, German language edition.

Deutsche Forschungsgemeinschaft (DFG) (1972) Mevinphos (Phosdrin) – MAK value documentation, German language edition.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) 2-Butenoic acid, 3-[(dimethoxyphosphinyl)oxy]-, methyl ester: Human health tier I assessment – IMAP report.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Phosdrin.

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