

PHORATE

CAS number: 298-02-2

Synonyms: O,O-Diethyl (S-ethylmercaptomethyl) dithiophosphate, o,o-diethyl (s-ethylthiomethyl) phosphorodithioate, granatox, rampart, thimet, timet

Chemical formula: $C_7H_{17}O_2PS_3$

Structural formula: —

Workplace exposure standard (amended)

TWA: 0.05 mg/m³ (5 ppb)

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 0.05 mg/m³ (5 ppb) is recommended to protect for cholinergic effects in exposed workers.

Insufficient data available to recommend a STEL. The previous STEL is recommended to be withdrawn.

Discussion and conclusions

Phorate is used as a contact insecticide and acaricide.

The critical effect of exposure is cholinesterase (ChE) inhibition, which results in cholinergic symptoms including decreased blood pressure, miosis, convulsions and coma (ACGIH, 2018; HCOTN, 2003).

Inhalational exposure data are limited and no quantitative human toxicological data are available. ChE inhibition is considered the most sensitive endpoint, which precedes cholinergic symptoms as demonstrated in rats and dogs (ACGIH, 2018; HCOTN, 2003). NOAEL of 0.05 and 0.07 mg/kg/day for red blood cells (RBC) and brain ChE inhibition in male and female rats, respectively, are reported in chronic feeding studies. This is supported by a NOAEL of 0.033 mg/kg/day for the same endpoints in a sub-chronic feeding rat study with a corresponding LOAEL of 0.1 mg/kg/day (ACGIH, 2018; HCOTN, 2003).

Due to the limited inhalational exposure data, ACGIH (2018) recommend a TWA equivalent of 0.05 mg/m³ based on the conversion of the sub-chronic NOAEL in rats to an inhalational equivalent of 0.2 mg/m³ (ACGIH, 2018). Following the same conversion, an inhalational equivalent of the LOAEL from this study would be 0.6 mg/m³.

In the absence of suitable inhalation exposure data, the recommended TWA of 0.05 mg/m³ by ACGIH (2018) is retained and expected to be protective of RBC ChE inhibition and subsequent cholinergic effects. There is insufficient evidence for cholinergic effects within an order of magnitude of the TWA. Therefore, the previous STEL of 0.2 mg/m³ is recommended to be withdrawn, which is supported by the withdrawal of the TLV-STEL by ACGIH (2018).

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.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 0.05 mg/m³; STEL: 0.2 mg/m³
Based on the recommendation by ACGIH (1991). Previous TLV-STEL of 0.2 mg/m ³ was withdrawn by ACGIH in 2004.		
ACGIH	2005	TLV-TWA: 5 ppb (0.05 mg/m³) (inhalable fraction and vapour)
<p>TLV-TWA intended to protect for cholinergic effects. Skin notation recommended based on dermal absorption and systemic poisoning in animals. Not classifiable as a human carcinogen based on negative results for carcinogenicity in chronic animal feedings studies.</p> <p>Summary of information</p> <p>No controlled human exposure data available.</p> <p>TLV-TWA based on NOAEL of 0.033 mg/kg/d for RBC ChE inhibition in rats. Assuming 100% absorption in a 70 kg individual with a respiratory volume of 10 m³ during an 8 h shift, an equivalent inhalational dose at the NOAEL is 0.2 mg/m³; TLV-TWA of 0.05 mg/m³ considered protective of RBC ChE inhibition and subsequent cholinergic effects.</p> <p>Particulate and vapour phase concentrations should be considered during monitoring to account for evaporative losses during sampling.</p> <p>Human data</p> <ul style="list-style-type: none"> • Case of accidental overexposure caused coma, miosis, frothy sputum, and convulsions; RBC and plasma ChE activities were 21 and 49% of baseline, respectively • Cholinergic effects in formulation workers (n=24/40, exposure details not provided) • Cholinergic symptoms in 2 workers in formulation plant at 0.07–14.6 mg/m³. <p>Animal data</p> <ul style="list-style-type: none"> • LD₅₀: 1.1–2.3 mg/kg (rats, oral) • LD₅₀: 2.5–6.2 mg/kg (rats, dermal) • LC₅₀: 11–60 mg/m³ (rats, 1 h); survivors recovered from cholinergic symptoms in 14 d • Rapid dermal absorption: 77% of dose excreted in urine, 12% in faeces within 24 h (rats) • Similar endpoint concentrations (for RBC ChE inhibition) reported in chronic and sub-chronic feeding/oral dose studies with rats and dogs - mice less sensitive: <ul style="list-style-type: none"> ○ NOAEL: 0.033 mg/kg/d feeding (rats, 13 wk), LOAEL: 0.1 mg/kg/d ○ NOAEL: 0.05 mg/kg/d oral dose (dogs, 6 d/wk, 13–15 wk); LOAEL: 0.25 mg/kg/d ○ NOAEL: 0.05 (females) and 0.15 mg/kg/d (males) feeding (rats, 2 yr); LOAEL: 0.15 (females) and 0.3 mg/kg/d (males), brain ChE inhibition also shown ○ NOAEL: 0.05 mg/kg/d oral dose (dogs, 1 yr); LOAEL: 0.25 mg/kg/d, brain ChE inhibition and slight tremor also observed ○ NOAEL: 0.9 mg/kg/d (highest tested dose) feeding (mice, 78 wk) • No evidence for carcinogenicity observed in chronic feeding studies (mice, rats, dogs) • Reproductive and developmental endpoints observed above endpoints for chronic toxicity: <ul style="list-style-type: none"> ○ reproductive NOAEL of 1.5 ppm (0.23 mg/kg/d) from a 3 generation mice study (0, 0.6, 1.5 and 3 ppm equivalent to 0, 0.09, 0.23 and 0.45 mg/kg/d); LOAEL of 3 ppm (0.45 mg/kg/d) based on viability and lactation index in repeat feeding study ○ NOAEL for both maternal and developmental was 0.25 mg/kg/d in a repeat gavage study (rats, GD 6–15, 0, 0.125, 0.25 and 0.5 mg/kg/d); LOAEL of 0.5 mg/kg/d for 		

Source	Year set	Standard
<p>maternal mortality, cholinergic effects and hypothermia, and foetal heart enlargement due to increased ChE producing excessive stimulation of myocardium</p> <ul style="list-style-type: none"> Non-genotoxic <i>in vitro</i>, no evidence for chromosomal aberrations <i>in vivo</i> (mice, rats); increased sister chromatid exchange reported in human lymphoblastoid cell line. <p>Insufficient data to recommend a TLV-STEL or sensitisation notation.</p>		
DFG	NA	NA
No report.		
SCOEL	NA	NA
No report.		
OARS/AIHA	NA	NA
No report.		
HCOTN	2003	TWA 8 hours: 0.05 mg/m³
<p>Summary of additional information:</p> <p>Current administrative OEL considered too high.</p> <p>Health-based recommended OEL (HBROEL) is derived from NOAEL of 0.07 mg/kg/d in chronic rat feeding study in the absence of quantitative short- or long-term inhalational exposure in animals and humans. Exposure duration is adjusted with a factor of 7/5, an allometric scaling factor of 4 for rats, and an overall factor of 9 to account for inter- and intraspecies differences are applied, which arrives at a human NAEL equivalent of 0.003 mg/kg/d. An inhalational equivalent of this NAEL, and thus the HBROEL, is 0.02 mg/m³.</p> <p>Animal data:</p> <ul style="list-style-type: none"> NOAEL: 0.05 (males) and 0.07 mg/kg/d (females) for brain ChE inhibition in chronic feeding study (rats, 2 yr, unclear if also cited in ACGIH, 2018). 		

Secondary source reports relied upon

Source	Year	Additional information
US NIOSH	✓ 2015	<ul style="list-style-type: none"> No quantitative dermal absorption studies available, capacity for systemic poisoning from dermal absorption inferred from acute dermal application studies (rats) High calculated ratio of skin dose to inhalation dose (SI): 3.3 Animal and workplace exposure studies indicate high toxicity, potential lethality, and ability to inhibit ChE from skin contact: <ul style="list-style-type: none"> 55–71% plasma ChE inhibition and bradycardia in 60% of exposed production plant workers (exposures not monitored, but involved both inhalation and dermal routes) Limited number of human patch tests did not suggest skin sensitization potential Composite skin notation of SK: SYS (FATAL) assigned.

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	Sk.
HCIS	—
NICNAS	—
EU Annex	—
ECHA	—
ACGIH	Carcinogenicity – A4, Skin
DFG	NA
SCOEL	NA
HCOTN	Skin
IARC	NA
US NIOSH	SK:SYS (Fatal)

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 LD₅₀ ≤1000 mg/kg: **yes**
 Dermal repeat-dose NOAEL ≤200 mg/kg:
 Dermal LD₅₀/Inhalation LD₅₀ <10: **yes**
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:	260.4
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m ³ ; 1 mg/m ³ = Number 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 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [TLVs® and BEIs® Guidelines section](#) on the ACGIH website.

Health Council of the Netherlands (HCOTN) (2003) Phorate. Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/075.

US National Institute for Occupational Safety and Health (NIOSH) (2011) Skin Notation Profiles: Phorate.