FONOFOS

CAS number: 944-22-9

Synonyms: Dyfonate, O-ethyl-S-phenylethylphosphonodithioate, ethylphosphonodithioic acid O-ethyl S-phenyl ester

Chemical formula: $C_{10}H_{15}OPS_2$

Structural formula: —

Workplace exposure standard (retained)

TWA: **0.01 ppm (0.1 mg/m^3)**

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 0.01 ppm (0.1 mg/m^3) is recommended to protect for cholinergic effects in exposed workers.

Discussion and conclusions

Fonofos is an organothiophosphate insecticide that was primarily used on corn, generally applied by ground equipment or aerial application.

The critical effect of exposure is red blood cell (RBC) cholinesterase (ChE) inhibition, which results in reversible neuromuscular stimulation and cardiorespiratory arrest at lethal concentrations. The human exposure data are limited to a case study of non-Hodgkin's lymphoma incidence and pesticide exposure and cases of accidental ingestion. Animal exposure data are limited to acute dose studies and a chronic feeding study of dogs, which reported a NOAEL of 0.2 mg/kg/day for RBC ChE inhibition with a corresponding LOAEL of 1.5 mg/kg/day.

In the absence of suitable human exposure data, the TWA of 0.1 mg/m^3 is based on a NOAEL of 0.2 mg/kg/day for RBC ChE inhibition in dogs as derived by ACGIH (2018). The recommended TWA of 0.1 mg/m^3 is considered sufficiently protective for the onset of cholinergic effects.

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 of dermal absorption and lethality in animals.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.1 mg/m^3***
ACGIH	***2006***	***TLV-TWA: 0.01 ppm (0.1 mg/m^3) inhalable fraction and vapour***

TLV-TWA intended to minimise potential for reversible cholinergic effects, e.g. neuromuscular stimulation.

Summary of data:

Human and animal inhalational exposure data are limited.

TLV-TWA derived from chronic feeding studies in dogs based on a NOAEL of 0.2 mg/kg/d and LOAEL of 1.58 mg/kg/d for RBC ChE inhibition in rats.

Inhalational equivalents of the NOAEL ≈1.4 mg/m^3 and LOAEL ≈10 mg/m^3 assuming 70 kg worker with respiratory volume of 10 m^3 during an 8 h shift; derived a TLV-TWA of 0.1 mg/m^3 presumably by applying a factor of 10 to the inhalation concentration of 1.4 mg/m^3 and rounded down to account for the steep dose-response relationship reported in animal studies; TLV-TWA therefore expected to be protective of cholinergic effects.

Summed particulate and vapour phase concentrations should be considered during sampling to account for evaporative losses.

BEI for RBC ChE inhibiting pesticides is available.

Human data:

- Accidental ingestion (unspecified amount) caused nausea, vomiting, salivation and sweating followed by cardiorespiratory arrest
  - patient was resuscitated and showed muscle fasciculation, low blood pressure and profuse salivary and bronchial secretion
  - recovery after treatment for 2 mo
- Case control study showed higher risk of non-Hodgkin's lymphoma associated with pesticide exposure, including Fonofos, for asthmatic individuals (OR=3.7) than for non-asthmatics (OR=1.6).

Animal data:

- Oral LD_{50}: 6.8–18.5 mg/kg (male rats); 3–8 mg/kg (female rats):
  - single lethal doses cause fasciculation, tremors, salivation and laboured breathing
  - autopsy shows lung erythema and congested liver, kidneys and adrenals
  - no such effects in survivors
- LC_{50}: 460 mg/m^3 (rats, 4 h), 900 mg/m^3 (rats, 1 h)
- Dermal LD_{50}: 25 mg/kg (rabbits), 147 mg/kg (rats), 278 mg/kg (guinea pigs):
  - lethal when instilled on eyes at 0.1 mL technical-grade (rabbits); no irritation noted
- Chronic feeding study with treatment groups 0.2, 1.5a and 12 mg/kg/d (dogs, 2 yr) reported:
  - NOAEL: 0.2 mg/kg/d
  - LOAEL: 1.5 mg/kg/d for moderate RBC ChE inhibition, increased liver weight, tremors, lachrymation and salivation; additional microscopic lesions in small intestine and liver reported at 12 mg/kg/d
  - similar cholinergic effects observed in 2 yr feeding study with rats; NOAEL: 0.5 mg/kg/d, LOAEL: 1.58 mg/kg for ChE inhibition

Source	Year set	Standard
		○ no evidence for carcinogenicity in both chronic feeding studies • Mutagenic *in vitro* with bacteria; no *in vivo* data reported • US EPA review of 3 generation reproductive feeding study, treatment range: 10–31.6 ppm in diet (rats, mice) reported: ○ foetal NOAEL: 1.58 mg/kg/d (rats) ○ foetal NOAEL: 2 mg/kg/d, foetal LOAEL: 6 mg/kg/d (mice) • 98% of orally absorbed substance excreted in urine and faeces within 96 h (rats); 0.38% in expired air. A skin notation is warranted based on low dermal LD_{50} values in animals. Not classifiable as a human carcinogen based on chronic animal feeding studies. Insufficient data to recommend a STEL or sensitiser notation.
DFG	***NA***	***NA***
No report.		
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
US EPA	✓	1987	• Chronic 2 yr feeding study (dogs) presented in ACGIH (2018) used as principal study to derive oral reference dose (RfD) • Chronic 2 yr rat feeding study not used to derive the RfD due to equivocal observations for ChE depression • Inhalation reference dose not yet established • Carcinogenic potential not yet evaluated.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Yes
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	—
ACGIH	Carcinogenicity – A4, Skin
DFG	NA
SCOEL	NA
HCOTN	NA
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	
Adverse effects in human case study:	
Dermal LD_{50} ≤1000 mg/kg:	yes
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD_{50}/Inhalation LD_{50} <10:	yes
In vivo dermal absorption rate >10%:	
Estimated dermal exposure at WES >10%:	
	consider assigning a skin notation

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	246.3
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 0.004 mg/m^3; 1 mg/m^3 = 250 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* on the ACGIH website.

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