

EPN

CAS number: 2104-64-5

Synonyms: O-Ethyl O-p-nitrophenyl phenylphosphonothioate,
O-Ethyl-O-(4-nitrophenyl) phenylthiophosphonate

Chemical formula: C₁₄H₁₄NO₄PS

Workplace exposure standard (amended)

TWA: 0.1 mg/m³

STEL: —

Peak limitation: —

Notations: Sk.

IDLH: 5 mg/m³

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 minimise potential for cholinergic symptoms in exposed workers.

Discussion and conclusions

EPN is an organophosphate pesticide used as a non-systemic insecticide and acaricide.

It affects cholinesterase (ChE) activity and has high oral toxicity with reports of acute poisoning and death following ingestion. Symptoms in humans included convulsions, cardio-respiratory arrest, coma, miosis, sweating, bloody stools, pulmonary oedema, tightness in the chest, fatigability, weakness, weight loss and muscle atrophy. Neurotoxic ataxia is reported in animal studies (ACGIH, 2018).

A NOEL for humans of 6 mg/kg/day is reported by DFG (2002). Based on an oral dose of 6 mg/kg/day which did not cause adverse effects in red blood cell (RBC) ChE activity in humans, a corresponding inhalation NOAEC exposure of 0.6 mg/m³ was determined by ACGIH (2018). Repeat dose oral exposure studies in rats and dogs reported that doses ranging between 0.25 to 1.0 mg/kg/day did not cause effects on RBC ChE activity (ACGIH, 2018). ACGIH assigned a TLV-TWA of 0.1 mg/m³ based on the NOAELs obtained in human and animal studies.

TWA of 0.1 mg/m³ as derived by ACGIH (2018) is recommended to protect for potential cholinergic effects in exposed workers.

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 lethality reported in animals following dermal application.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 0.5 mg/m³
ACGIH	2003	TLV-TWA: 0.1 mg/m³
<p>TLV-TWA recommended to prevent occurrence of cholinergic symptoms and other adverse biological effects (decreased activity of ChE enzymes) in exposed workers. Potency seen in humans considered similar to rats (no affect at RBC cholinesterase at 0.25 mg/kg) and dogs (0.1 mg/kg/d). TLV-TWA is derived from a NOAEL obtained in humans and in animals.</p> <p>Both particulate and vapour phase concentrations should be considered and combined to determine total airborne concentrations.</p> <p>Summary of data:</p> <p>EPN is no longer registered for use.</p> <p>Human data:</p> <ul style="list-style-type: none"> • Coma, miosis, sweating, bloody stools, pulmonary oedema and death reported in 1 case following accidental ingestion of estimated 200 mL of 50% EPN • Death, preceded by convulsions and cardio-respiratory arrest, reported in farmer following 500 mL suspension containing EPN (collected from GIT) • Symptoms of EPN poisoning include tightness in the chest, fatigability, weakness, weight loss, muscle atrophy and optical media discolouration • No cholinergic symptoms reported in workers following respiratory exposures at 11–317 µg/d and dermal exposures of 2.1–117.7 mg/d • Oral administration in volunteers of 0.13 mg/kg/d for 56 d resulted in inhibition of plasma ChE activity 2 wk following administration and continued 3 wk following cessation of dosing <ul style="list-style-type: none"> ○ RBC ChE inhibition also occurred to a similar extent but later than plasma • Oral administration in volunteers of 0.086 mg/kg/d for 47 d did not have any significant effect on plasma or RBC ChE activity and no clinical effects reported • Oral administration in volunteers of 0.086 mg/kg/d plus 0.23 mg/kg/d malathion for 44 d resulted in significant inhibition of both RBC and plasma ChE with authors suggesting detoxification of malathion is inhibited by EPN. <p>Animal data:</p> <ul style="list-style-type: none"> • LC₅₀: 106 mg/m³ (rats, inhalation, 1 h) • LD₅₀: 25 mg/kg (rats, dermal) and 65 mg/kg (rats, oral gavage) • Administered in combination, EPN greatly potentiates malathion toxicity with 10-fold potentiation observed in rats and ~50-fold in dogs • 25 ppm (1.25 mg/kg/d) in diet of rats for 90 d caused significant inhibition of RBC ChE activity with no adverse effects noted at 5 ppm (0.25 mg/kg/d) • Neurotoxic ataxia reported in hens following oral doses of 0.1–5.0 mg/kg/d for 90 d and no signs of ataxia at 0.01 mg/kg/d • Dogs treated orally for 90 days (capsule, doses of up to 3 mg/kg/d) showed no effects at 1 mg/kg/d except plasma cholinesterase activity but at 3 mg/kg/d showed: <ul style="list-style-type: none"> ○ decreased RBC and brain cholinesterase activity ○ decreased RBC, haemoglobin and haematocrit in both sexes ○ pancreatic acinar cell atrophy in 2 males ○ affected by dietary dose of 2 mg/kg but not at 0.5 mg/kg and 0.1 mg/kg 		

Source	Year set	Standard
<ul style="list-style-type: none"> Lifetime testing in rats did not cause increase in tumours No mutagenic response in strains of <i>S. typhimurium</i> or reversion assays in <i>E. coli</i> Readily absorbed following dermal or oral exposure. <p>A skin notation is assigned based on lethality in rabbits following dermal application at relatively low doses.</p> <p>Insufficient data in humans and animals to recommend SEN notation or TLV-STEL.</p> <p>Not classified as human carcinogen.</p>		
DFG	2002	MAK: 0.5 mg/m³
<p>MAK assigned in 1958.</p> <p>Summary of additional data:</p> <ul style="list-style-type: none"> LOEL not specified, NOEL for humans 6 mg/kg/d (no further information) Cholinesterase enzyme inhibition is initially reversible, therefore concentration-dependent. 		
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	<ul style="list-style-type: none"> Inhalation RfC not evaluated
US NIOSH	✓ 2007	<ul style="list-style-type: none"> TWA 0.5 mg/m³ (skin)

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	Skin
HCIS	—
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A4, Skin

Source	Notations
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
Dermal LD ₅₀ ≤ 1000 mg/kg:	yes
Dermal repeat-dose NOAEL ≤ 200 mg/kg:	
Dermal LD ₅₀ /Inhalation LD ₅₀ < 10:	yes
<i>In vivo</i> dermal absorption rate > 10%:	
Estimated dermal exposure at WES > 10%:	
a skin notation is warranted	

IDLH

Is there a suitable IDLH value available? Yes

Additional information

Molecular weight:	323.31
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.

Deutsche Forschungsgemeinschaft (DFG) (2002) EPN (O-Ethyl-O-(4-nitrophenyl) phenylthiophosphonat – MAK value documentation.

US Environmental Protection Authority (US EPA) (1987) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Ethyl p-nitrophenyl phenylphosphorothioate (EPN); CASRN 2104-64-5.

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

US National Institute for Occupational Safety and Health (NIOSH) (2007) NIOSH Pocket Guide to Chemical Hazards – EPN.

US National Institute for Occupational Safety and Health (NIOSH) (2017) NIOSH Skin Notation Profiles: Ethyl p-nitrophenyl phenylphosphorothioate (EPN).