

NALED

CAS number: 300-76-5

Synonyms: Bromclopophos, Bromix®, Dibrom®, dimethyl-1,2-dibromo-2,2-dichloroethyl phosphate, Ortho 4355®, phosphoric acid 1,2-dibromo-2,2-dichloroethyl dimethyl ester

Chemical formula: $C_4H_7Br_2Cl_2O_4P$

Structural formula: —

Workplace exposure standard (amended)

TWA: 0.1 mg/m³

STEL: —

Peak limitation: —

Notations: Sk.

IDLH: 200 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 protect for cholinesterase inhibition in exposed workers.

Discussion and conclusions

Naled is an organophosphate insecticide used to control mosquitos and other insects in field crops and plants.

The critical effect from exposure is decreased activity of cholinesterase enzymes.

Data in humans are limited. Cases of allergic dermatitis are reported in horticulture workers. A NOAEC of 0.2 mg/m³ is reported in rats from a thirteen-week inhalation study and was used in the recommendation of OEL by ACGIH (2018) and HCOTN (2003). The DFG (2017) used a calculated benchmark dose of 2 mg/m³ from the same thirteen-week inhalation study in rats to derive the MAK value of 0.5 mg/m³. A five-week inhalation study in guinea pigs and rats reported observations of red blood cell (RBC) and brain cholinesterase inhibition at greater than 1.7 mg/m³. A NOAEL of 0.2 mg/kg/day was noted in a one-year gavage study in dogs and in a two-year gavage study in rats for plasma, RBC and brain cholinesterase inhibition activities. This NOAEL was calculated to be equivalent to a human inhalation dose at 1.5 mg/m³ using generic factors and was used to support the derivation of the TWA (ACGIH, 2018).

A TWA of 0.1 mg/m³ is recommended based on the weight of evidence and as assigned by ACGIH (2018). This TWA is expected to be protective of inhibition of the cholinesterase activity as observed in animals.

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 review of the dermal sensitiser classification is recommended based on evidence in workers.

A skin notation is recommended based on evidence in humans and animals.

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APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 3 mg/m³
ACGIH	2014	TLV-TWA: 0.1 mg/m³, inhalable fraction and vapor
<p>TLV-TWA (inhalable fraction and vapor) recommended to minimise for cholinergic and other adverse effects.</p> <p>Summary of data:</p> <ul style="list-style-type: none"> • TLV-TWA recommendation stated based on the following evidence: <ul style="list-style-type: none"> ○ brain cholinesterase activity inhibited in rats following exposures at 6 mg/m³ but not at 1 mg/m³ (13-wk inhalation study) ○ plasma and RBC enzyme activity was inhibited in rats at 1 mg/m³ but not at 0.2 mg/m³ (13-wk inhalation study) ○ inhibition of RBC and brain cholinesterase activity in guinea pigs and rats at ≥1.7 mg/m³ (6 h/d, 5 d/wk for 5 wk) ○ NOAEL of ~0.2 mg/kg/d in dogs (1 yr gavage) and rats (2 yr gavage) for plasma, RBC, and brain cholinesterase activities; ≡human inhalation dose of 1.5 mg/m³; assuming 70 kg worker breathing 10 m³ per 8-h shift and 100% absorption. <p>Human data:</p> <ul style="list-style-type: none"> • Symptoms associated with accidental or intentional poisoning (no exposure/dose data provided) include: <ul style="list-style-type: none"> ○ abdominal cramps, emesis, nausea, hypersecretion, cough, and perspiration that disappeared after 2 d ○ anxiety, depression, vertigo, and spontaneous horizontal nystagmus that continued for 4 mo • Report of contact sensitisation-type dermatitis in horticultural workers; no further information • Report of contact dermatitis in an aerial applicator • Dermatitis reported to be caused by picking flowers sprayed with Naled • No further human data. <p>Animal data:</p> <ul style="list-style-type: none"> • 4-h LC₅₀ in rats: 190 mg/m³ females; 200 mg/m³ males • LD₅₀: 800 mg/kg (rats, dermal) • Rats exposed for 6 h/d, 5 d/wk for 13-wk at 0, 0.2, 1, or 6 mg/m³: <ul style="list-style-type: none"> ○ 0.2 mg/m³ no plasma and RBC cholinesterase inhibition observed (cited as NOAEC by HCOTN, 2003) ○ 1 mg/m³ and 6 mg/m³ plasma and RBC cholinesterase inhibited ○ 6 mg/m³ resulted in signs of cholinergic toxicity (tremors, salivation, nasal discharge, abnormal respiration, anogenital staining) ○ 6 mg/m³ brain cholinesterase inhibition • Inhibition of RBC and brain cholinesterase activity in guinea pigs and rats at ≥1.7 mg/m³ (6 h/d, 5 d/wk for 5 wk) • Dogs dosed at 0, 0.2, 2.0 or 20 mg/kg/d <i>via</i> gavage for 1-yr: 		



Source	Year set	Standard
<ul style="list-style-type: none"> plasma, RBC, and brain cholinesterase activities were depressed at 2.0 and 20 mg/kg/d; brain was depressed at 2 mg/kg/day in females only clinical signs (emesis, diarrhoea) and statistically significant increases in mineralisation of the lumbar spinal cord in both sexes at doses of 2 and 20 mg/kg/d mild testicular degeneration in males associated with 2 and 20 mg/kg/d NOAEL noted as 2 mg/kg/d from this study in derivation of TWA; no further information Rats dosed at 0, 0.2, 2 or 10 mg/kg/d <i>via</i> gavage for 2 yr: <ul style="list-style-type: none"> no cholinesterase effects at 0.2 mg/kg/d; noted as NOAEL for derivation TWA dose related reduction in plasma, brain and RBC cholinesterase activity in 2 or 10 mg/kg/d groups slight tremors were noted on isolated occasions after dosing in 4 females given 10 mg/kg/d NOAEL of ~0.2 mg/kg in dogs (1 yr gavage) and rats (2 yr gavage); plasma, RBC, and brain cholinesterase activities; \approx human inhalation dose 1.5 mg/m³; assuming 70 kg worker breathing 10 m³ per 8 h shift and 100% absorption Positive for gene mutation in the <i>S typhimurium</i> reverse mutation assay. <p>Insufficient data for RSEN notation and TLV-STEL recommendation.</p>		
DFG	2017	MAK: 0.5 mg/m³
<p>MAK recommended to minimise cholinesterase activity effects.</p> <p>Summary of data:</p> <p>Human Data:</p> <ul style="list-style-type: none"> No additional data. <p>Animal Data:</p> <ul style="list-style-type: none"> Reported BMDL of 2 mg/m³ for 30% inhibition; based on 13 wk study in rats (cited by ACGIH, 2014); inhibition of cholinesterase activity in erythrocytes and the brain MAK based on BMDL factor of 2 for extrapolation from animals to humans and taking into consideration the higher respiratory volume at the workplace in comparison with test animals (no further information) NOAEL 8 mg/kg/d in rats for developmental toxicity; no further information. 		
SCOEL	NA	NA
No report.		
OARS/AIHA	NA	NA
No report.		
HCOTN	2003	TWA: 3 mg/m³
<p>TWA is an administrative OEL; recommends a health-based OEL (HBROEL) TWA of 0.02 mg/m³ for inhibition of RBC AChE.</p> <p>Summary of data:</p> <p>Human Data:</p> <ul style="list-style-type: none"> No additional data. <p>Animal Data:</p> <ul style="list-style-type: none"> Basis for recommended TWA (0.02 mg/m³): <ul style="list-style-type: none"> NOAEC of 0.2 mg/m³ reported in rats 13 wk inhalation study (cited by ACGIH, 2014) 		

Source	Year set	Standard
		<ul style="list-style-type: none"> ○ UF of 9 to account for intra-and interspecies variation • Dermal NOAEL for both brain and red blood cell AChE inhibition was reported as 1 mg/kg/d in rats.

Secondary source reports relied upon

NIL.

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, DSEN, Skin
DFG	Sh (dermal sensitiser), H (skin)
SCOEL	NA
HCOTN	Skin
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:	yes
Dermal LD ₅₀ ≤1000 mg/kg:	yes
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD ₅₀ /Inhalation LD ₅₀ <10:	
<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:	380.78
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) (2019) Naled – MAK value documentation.

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).

Health Council of the Netherlands (HCOTN) (2000) Naled. Health-based reassessment of administrative occupational exposure limits. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/074.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Dimethyl-1,2-dibromo-2,2-dichlorethyl phosphate (Naled).

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