

DEMETON

CAS number: 8065-48-3

Synonyms: Demox, Mercaptofos, Systox

Chemical formula: $C_8H_{19}O_3PS_2$

Structural formula: —

Workplace exposure standard (retained)

TWA: 0.01 ppm (0.1 mg/m³)

STEL: —

Peak limitation: —

Notations: Sk.

IDLH: 10 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 0.01 ppm (0.1 mg/m³) is recommended to protect for neurotoxic cholinergic effects in exposed workers.

Discussion and conclusions

Demeton has historical uses as an insecticide, with use discontinued in several countries (ACGIH, 2018; HCOTN, 2003).

It is highly neurotoxic and critically affects cholinesterase activity. At higher concentrations it causes lachrymation, muscular fits and cramps, nausea and paralysis (DFG, 2003).

Inhibition of acetyl cholinesterase is considered the most sensitive critical effect. A NOAEL of 0.05 mg/kg for cholinesterase inhibition, but no clinical effects, is reported in a repeat dose volunteer study (ACGIH, 2018). Interpolation of the NOAEL from continuous exposure to a five day work week by multiplication with a factor of 7/5 yields 0.07 mg/kg. To account for interindividual variation and translation from experimental to workplace exposure, an uncertainty factor of six is applied to afford a NOAEL of 0.01 mg/kg. Therefore, the recommended TWA of 0.1 mg/m³ achieves an effective dose at this NOAEL, assuming a 70 kilogram worker with a respiratory rate of 10 m³ per eight hour shift (HCOTN, 2003).

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 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 (0.11 mg/m³)
ACGIH	2002	TLV-TWA: 0.005 ppm (0.05 mg/m³)
<p>TLV-TWA intended to protect for cholinergic effects and derived from volunteer repeat oral dose study with NOAEL of 0.06 mg/kg/d; corresponding LOAEL was 0.10 mg/kg. Findings of human study supported by animal studies with comparable NOAELs.</p> <p>A skin notation is assigned due to systemic effects observed in animals given low dermal doses. Insufficient data to recommend a STEL, or notations for carcinogenicity or sensitisation.</p> <p>Summary of data:</p> <p>Demeton is a highly toxic 2:1 mixture of two phosphorothioate isomers (Demeton-S, Demeton-O). Neurotoxicity is characterised by cholinesterase inhibition. Metabolic oxidation produces more potent cholinesterase inhibitors than Demeton.</p> <p>Human data:</p> <ul style="list-style-type: none"> Accidental overexposure to skin (60 mL of concentrate spilled on clothing, no further details) led to nausea, vomiting and weakness for 9 h in one case No clinical evidence of poisoning but decreased blood cholinesterase in 12/14 workers exposed to 1 mg/m³ (duration not specified) <ul style="list-style-type: none"> similar report from another study at 6 mg/m³ (no further information provided) Volunteer repeat oral dose study (n=5, 30 d exposure, 30 d pre/post observation), treatment range: 0.06–0.10 mg/kg/d; response measured by plasma and blood cholinesterase activity: <ul style="list-style-type: none"> NOAEL: 0.06 mg/kg/d for cholinesterase inhibition and clinical signs of toxicity LOAEL: 0.10 mg/kg/d; 40% inhibition within 25 d 1 subject experienced inhibition at 0.06 mg/kg/d within 24 d no clinical signs of toxicity in any subjects. <p>Animal data:</p> <ul style="list-style-type: none"> LD₅₀: 6.2–8.0 mg/kg (male rats, oral), 2.5 mg/kg (female rats, oral) LD₅₀: 3.0 mg/kg (rats, intraperitoneal) LD₅₀: 8.2 and 14 mg/kg (female and male rats respectively, neat, dermal); toxicity varies greatly depending on formulation: <ul style="list-style-type: none"> 50% in emulsifier LD₅₀: 620 mg/kg spray formulation: LD₅₀: 5 mg/kg LC₅₀: 175 mg/m³ (rats, 1 h), 47 mg/m³ (rats, 4 h) No signs of illness at 3 mg/m³ after (rats, 2 h); second exposure caused tremors, third exposure caused severe tremors and lachrymation, fourth exposure was lethal Several subchronic feeding studies with rabbits, rats and dogs indicate dose-dependent cholinesterase inhibition, which was lethal to rabbits above 0.5 mg/kg (rabbits, 64 d): <ul style="list-style-type: none"> NOAEL: 0.1–0.15 mg/kg (rabbits, 98–106 d) LOAEL: 0.05 mg/kg (rats, 11–16 wk) NOAEL: 0.025 mg/kg (dogs, 24 wk) Embryotoxic at 7–10 mg/kg when administered to mice GD 7–12; decreased foetal weight and slightly higher mortality 		

Source	Year set	Standard
<ul style="list-style-type: none"> No mutagenicity data presented; preliminarily grouped with structurally similar Disulfoton, which exhibits equivocal mutagenicity. <p>A skin notation is assigned due to systemic effects observed in animals given low dermal doses. Insufficient data to recommend a STEL, notations for carcinogenicity or sensitisation.</p>		
DFG	2003	Not established
<p>Summary of additional data:</p> <p>MAK withdrawn due to insufficient information on mechanism of toxicity in humans. Adverse effects expected to present at >30% blood AChE inhibition. Critical effects are difficulty focussing, salivation, lachrymation, muscular fits and cramps, gastrointestinal disturbance, nausea, weakness and paralysis; death occurs from respiratory arrest and heart failure.</p> <p>No information on the carcinogenic potential, mutagenicity data is equivocal.</p> <p>Skin notation retained due to high dermal toxicity in rats. Insufficient data to recommend a sensitiser notation.</p> <p>Human data:</p> <ul style="list-style-type: none"> Restricted breathing and whistling noises in cases of accidental inhalation (concentration and duration not specified). <p>Animal data:</p> <ul style="list-style-type: none"> Some evidence for habituation in high exposure groups of repeat feeding studies with rats (also cited in ACGIH, 2018) NOAEL: 0.5 mg/kg/d for cholinesterase inhibition in repeat feeding study (guinea pigs, 6 d/wk, 8 wk); LOAEL: 5 mg/kg Equivocal mutagenicity data presented: <ul style="list-style-type: none"> increased SCE in V79 cells dose-dependent chromosomal aberrations in bone marrow of IP injected hamsters; NOAEL: 1 mg/kg, LOAEL: 2 mg/kg produces no dominant lethal mutations in mice at 2 mg/kg (1/d, 1–5 d). 		
SCOEL	NA	NA
No report.		
OARS/AIHA	NA	NA
No report.		
HCOTN	2003	TWA: 0.1 mg/m³
<p>Summary of additional data:</p> <p>Existing administrative 8-h TWA is 0.1 mg/m³ with skin notation. Inhibition of AChE considered most sensitive critical effect.</p> <p>Health-based TWA derived from NOAEL of 0.05 mg/kg in continuous repeat dose volunteer study. Multiplication of the NOAEL by 7/5, for interpolation to 5 d work exposure from 7 d continuous study, yields 0.07 mg/kg. An overall assessment factor of 6 is applied to account for interindividual variation and confidence in the database to afford a NOAEL of 0.01 mg/kg which is recommended as the health-based TWA.</p> <p>Not expected to accumulate in tissue based on rapid metabolism of Disulfoton, of which Demeton-S is a metabolite.</p> <p>No carcinogenicity studies available for assessment, but no carcinogenic activity observed.</p> <p>Human data:</p> <ul style="list-style-type: none"> Accidental fatal exposure when crop-dusting aeroplane was cleaned 		

Source	Year set	Standard
<ul style="list-style-type: none"> Accidental overexposure of a young male led to weakness, difficulty breathing, unconsciousness; autonomic nervous effects were observed 3 mo post-exposure Volunteer repeat dose study (cited in ACGIH, 2018) used to support TWA derivation. <p>Animal data:</p> <ul style="list-style-type: none"> <i>In vitro</i> mutagenicity demonstrated, but <i>in vivo</i> mutagenicity data not available for assessment. 		

Secondary source reports relied upon

Source	Year	Additional information
US EPA	✓ 2002	<ul style="list-style-type: none"> Carcinogenicity not yet assessed.
US NIOSH	✓ 1994	<ul style="list-style-type: none"> IDLH of 10 mg/m³ not derived experimentally; based on an analogy with AChE inhibitor, parathion, which has an IDLH of 10 mg/m³.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Insufficient data

Is the chemical carcinogenic with a mutagenic mechanism of action? Insufficient data

Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	Skin
HCIS	—
NICNAS	NA
EU Annex	—
ECHA	NA
ACGIH	Skin
DFG	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 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? Yes

Additional information

Molecular weight:	230.28
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 10.6 mg/m ³ ; 1 mg/m ³ = 0.09 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) (2012) Demeton – MAK value documentation.

Health Council of the Netherlands (HCOTN) (2003) Demeton. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/068.

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

US Environmental Protection Authority (US EPA) (2002) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Demeton.