

MALATHION

CAS number: 121-75-5

Synonyms: Carbophos, O,O-dimethyl dithiophosphatediethyl mercaptosuccinate, O,O-dimethyl-S-(1,2-dicarbethoxyethyl)phosphorodithioate, maidison, mercaptothion

Chemical formula: $C_{10}H_{19}O_6PS_2$

Workplace exposure standard (amended)

TWA: 1 mg/m³

STEL: —

Peak limitation: —

Notations: Sk., DSEN

IDLH: 250 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 1 mg/m³ is recommended to protect for cholinergic effects in exposed workers.

Discussion and conclusions

Malathion is used as a broad-spectrum pesticide. Use in Australia is heavily restricted.

Critical effects of exposure include red blood cell (RBC) cholinesterase (ChE) inhibition and adverse central nervous system (CNS) effects at higher concentrations. These systemic effects are also demonstrated in humans following dermal exposure (ACGIH, 2018).

Human inhalational exposure data are limited. A NOAEL of 16 mg per day for RBC ChE inhibition is reported in volunteers given oral doses in a sub-chronic study. This dose extrapolates to an equivalent NOAEC of 1.6 mg/m³ (ACGIH, 2018). ACGIH (2018) used this NOAEC to derive a TLV-TWA of 1 mg/m³ which is recommended to be adopted. The recommended TWA is expected to be protective of cholinergic effects as observed in orally dosed humans.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Equivocal evaluations of carcinogenic potential in animals have led to inconsistencies in the recommended carcinogenicity notations by the ACGIH (2018) and IARC (2017). Strong evidence for genotoxicity is also reported by the IARC (2017). However, evidence for carcinogenicity in humans is inconclusive and it is recommended that the classification be reviewed.

Classified as a skin sensitiser and not a respiratory sensitiser according to the GHS.

A skin notation is recommended based on evidence of dermal absorption and adverse systemic effects in humans.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 10 mg/m³
ACGIH	2003	TLV-TWA: 1 mg/m³ (inhalable aerosol and vapor)
<p>TLV-TWA intended to protect for cholinergic effects.</p> <p>Summary of data:</p> <p>TLV-TWA recommended for high purity forms of the substance; impurities or exposures to other pesticides may increase the toxicity of malathion due to inhibition of the detoxification pathway for the active metabolite, malaoxon.</p> <p>TLV-TWA derived from a NOAEL of 16 mg/d for RBC ChE inhibition in volunteers, equates to an air concentration of 1.6 mg/m³ assuming a respiratory volume of 10 m³ during an 8 h shift.</p> <p>Human data:</p> <ul style="list-style-type: none"> • Overexposures by ingestion or dermal application cause unconsciousness and convulsions • 90% of IV dose excreted in urine within 5 d <ul style="list-style-type: none"> ◦ elimination half-life: 3 h ◦ 8% of a dermal dose (4 µg/cm²) absorbed in 120 h in volunteer; <i>in vitro</i> 0.6–4% or 8% absorbed from cotton or ethanol solution, respectively • Case study of poisonings of insecticide sprayers (n=2,810) estimated dermal exposures between 1–200 µg/cm²; exposure was likely to impure malathion <ul style="list-style-type: none"> ◦ peak inhalational concentrations were measured at ≈1.5 mg/m³ but considered less causal of intoxication: ◦ pure malathion formulations caused 0.8–3% RBC ChE inhibition, contaminated formulations caused 2–3% inhibition • No cholinergic effects observed during aerial spraying events <ul style="list-style-type: none"> ◦ maximum chronic dose rates estimated at 246 µg/kg/d (dermal), 0.1 µg/kg/d (inhalational), 80 µg/kg/d (ingestion) • No cholinergic effects reported in workers exposed to total 4.9–11.3 mg/d for 2 wk <i>via</i> inhalation (average 0.5–4 mg/m³, peak 56 mg/m³, up to 30 min/d) and dermal contact (0.05–0.13 mg/kg/d) • NOAEL: 16 mg/d ≈0.23 mg/kg/d for RBC ChE inhibition in repeat oral dose study (males, n=5, 32–56 d) <ul style="list-style-type: none"> ◦ LOAEL of 24 mg/d caused 20% ChE inhibition • No cholinergic symptoms, including ChE inhibition at up to 85 mg/m³ (males, n=4, 1 h, 2 times/d, 42 d) <ul style="list-style-type: none"> ◦ agency calculates equivalent 8 h exposure as 21 mg/m³, which would be expected to elicit cholinergic effects observed above the cited oral dose NOAEL. <p>Animal data:</p> <ul style="list-style-type: none"> • Oral LD₅₀: 1,000–1,375 mg/kg (rats); Dermal LD₅₀ >4,444 mg/kg (rats), systemic cholinergic effects were observed at non-lethal doses, impure substance or mixed exposure with other pesticides increases toxicity • LC₅₀ >5,200 mg/m³ (rats, 4 h); cholinergic effects reported including restlessness, defecation, lachrymation, tremors, muscular fibrillations 		



Source	Year set	Standard
		<ul style="list-style-type: none">• Non-sensitising to skin (guinea pigs, no further information provided)• NOAEL: 50 mg/kg/d for plasma, brain and RBC ChE inhibition in repeat dermal application study (rabbits, 6 h/d, 21 d); LOAEL: 300 mg/kg/d• Overall, results of several chronic feeding studies are suggestive of carcinogenicity in animals, but insufficient to relate these effects to humans:<ul style="list-style-type: none">○ liver tumours were induced in mice at high concentrations ($\approx 1,500$ mg/kg/d) that also caused liver hypertrophy○ no statistically significant increase in tumours in rats fed malaoxon (≈ 128 mg/kg/d)• Considered non-genotoxic; high concentrations of technical grade and pure substance are weakly mutagenic <i>in vitro</i> at cytotoxic concentrations. <p>Insufficient data available to recommend a TLV-STEL or a sensitiser notation.</p> <p>A skin notation is recommended based on reports of systemic poisoning in humans from dermal application.</p> <p>Chronic exposure studies in animals or case studies in humans do not clearly indicate carcinogenic potential; not classified human carcinogen.</p>
DFG	2007	MAK: 15 mg/m ³
		<p>Summary of additional data:</p> <p>Human exposure database too weak to derive MAK; instead based on weight of evidence from industrial experience that has not led to increased inhalation-related cases of intoxication since its establishment (1958). Adverse reproductive effects observed >100 and 300 mg/kg/d in rabbits and rats, respectively; not expected to occur at the MAK of 15 mg/m³, which equates to inhalational exposure at $2,100$ mg/m³.</p> <p>Human data:</p> <ul style="list-style-type: none">• Odour threshold for technical grade substance: 0.044 mg/m³• Changes in ChE activity in 12 production workers (no further details provided)• Aerial spraying did not cause adverse effects in exposed individuals, average air concentrations range: 0.6–2 mg/m³ (duration not specified)• Slight eye and nose irritation at 85 mg/m³ in volunteers exposed by inhalation (also cited in ACGIH, 2018). <p>Animal data:</p> <ul style="list-style-type: none">• 60% absorbed through skin (rat); 23% of oral dose recovered in urine within 16 h• NOAEC: 0.014 mg/m³ for pericellular oedema in CNS in continuous inhalation study (rats, 24 h/d, 7 d/wk, 3 mo)<ul style="list-style-type: none">○ LOAEC 0.075 mg/m³• NOAEL: 100 ppm in diet for ChE inhibition in several continuous feeding studies (rats, dogs, 12 wk to 2 yr)• No embryotoxic effects at maternally toxic levels of 600–900 mg/kg ip injection in developmental study (rats, on gestation d 11)• Decreased litter size and viability at toxic doses of 240 mg/kg in repeat oral reproductive study (rats, 5 mo). <p>Carcinogenicity, skin absorption and sensitisation potential not assessed.</p>

Source	Year set	Standard
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
NICNAS	* 2018	<ul style="list-style-type: none"> • Tier I: not assessed due to agricultural use.
IARC	✓ 2017	<ul style="list-style-type: none"> • Comet assay showed increased rates of DNA damage in blood lymphocytes in exposed workers • Increased chromosomal aberrations in peripheral blood lymphocytes of exposed workers • Based on review of mechanistic studies, a Group 2A classification is supported, as these mechanisms can potentially operate in humans: <ul style="list-style-type: none"> ○ strong evidence that malathion-based pesticides are genotoxic in humans and animals ○ strong evidence for alteration of cell proliferation and tumour cell receptor interactions in thyroid and breasts ○ strong evidence for inflammation due to excess oxidative stress ○ limited evidence for positive association with non-Hodgkin lymphoma and cancer of the prostate incidence in humans. • Sufficient evidence for carcinogenicity in animals • Substance probably carcinogenic to humans (Group 2A) • Malathion was found to be a weak contact sensitizer, inducing mild cutaneous reaction in high proportion of subjects.
US EPA	✓ 1987	<ul style="list-style-type: none"> • Oral RfD derived principally from repeat oral dose study in volunteers with NOAEL of 16 mg/kg/d (also cited in ACGIH, 2018) • Carcinogenic potential not yet assessed.
US NIOSH	✓ 1994	<ul style="list-style-type: none"> • IDLH based on acute toxicity data in humans.

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	—
HCIS	Skin sensitisation – category 1
NICNAS	NA
EU Annex	Skin sensitisation – category 1
ECHA	NA
ACGIH	Carcinogenicity – A4, Skin
DFG	—
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 2A
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

Conclusion:

Adverse effects in human case study:

yes

Dermal LD₅₀ ≤ 1000 mg/kg:

Dermal repeat-dose NOAEL ≤ 200 mg/kg:

Dermal LD₅₀/Inhalation LD₅₀ < 10:

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:	330.36
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:	✓
This chemical is a biological product:	<input type="checkbox"/>



Molecular weight:	330.36
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 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) (2007) Malathion – MAK value documentation.

International Agency for Research on Cancer (IARC) (2017) Some organophosphate insecticides and herbicides. IARC Monographs on the evaluation of the carcinogenic risk to humans, volume 112.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) Butanedioic acid, [(dimethoxyphosphinothioyl)thio]-, diethyl ester: Human health tier I assessment – IMAP report.

Tenth Adaptation to Technical Progress Commission Regulation (EU) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

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