AZINPHOS-METHYL

CAS number:	86-50-0
Synonyms:	Gusathion, gusathion A, Guthion®, O,O-dimethyl S-[(4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl]dithiophosphate, phosphorodithioic acid, O,O-dimethyl S-[(4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl] ester
Chemical formula:	$C_{10}H_{12}N_3O_3PS_2$

Workplace exposure standard (amended)

TWA:	**1 mg/m^3**
STEL:	**—**
Peak limitation:	**—**
Notations:	**Sk.; DSEN**
IDLH:	**10 mg/m^3**
Sampling and analysis:	The recommended value is readily quantifiable through currently available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 1 mg/m^3 is recommended to protect for adverse effects resulting from the inhibition of acetylcholinesterase (AChE) in exposed workers.

Discussion and conclusions

Azinphos-methyl is a broad-spectrum organophosphate insecticide with a toxic mode of action due to inhibition of AChE. It has been reported to be readily absorbed across the skin of humans and animals causing systemic effects (ACGIH, 2018; DFG, 2019).

Several NOAEL ranges from animal (0.16 mg/kg/d to 0.75 mg/kg/d from one- and two-year feeding studies) and human studies (0.25 to 0.29 mg/kg/d from 28 and 30 day oral studies) have been reported. The reported oral NOAEL doses are converted to inhalation concentrations by applying generic human exposure factors. These conversions to inhalational exposures ranged from 1.12 to 1.84 mg/m^3 (three animal studies), and approximately 1.75 to 2.03 mg/m^3 (three human volunteer studies) (DFG, 2019). On a weight of evidence, considering the available animal and human studies, the lowest value is used to recommend a TWA of 1 mg/m^3. The recommended TWA is considered protective for the critical effects of AChE inhibition in the exposed workers.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

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 resulting in systemic effects in humans and animals.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.2 mg/m³***
ACGIH	***2014***	***TLV-TWA: 0.2 mg/m³***

TLV-TWA recommended to protect for decreased activity of AChE and other biological effects in exposed workers.

Summary of data:

Human data:

- Case report of visual disturbances, headache, tightness of chest, abdominal cramps, nausea, vomiting, weakness and excess salivation in a male who spilled concentrate on their hands
- No adverse cholinergic effects or AChE inhibition compared to pre-exposure levels in volunteers given repeated oral dose of 0.23 mg/kg
- TLV-TWA of 0.2 mg/m^3 was derived using the oral dose of 0.23 mg/kg and converting it to an inhalational exposure of 1.6 mg/m^3 for 8 h working shift (assuming 70 kg bw breathing 10 m^3 with 100% absorption)
- Observational studies reported 70% reduction in blood AChE activity in workers working in treated orchards with dermal intake being the primary exposure route.

Animal data:

- LC_{50}: 132–155 mg/m^3 (female rats, 4 h, 14 d)
- LC_{50}: 385–396 mg/m^3 (male rats, 1 h, 14 d)
- Rats exposed at ≤4.72 mg/m^3 for 6 h/d, 5 d/wk for 12 wk:
  - no significant changes in appearance or behaviour
  - reduced body weight gains in males at 4.72 mg/m^3
  - inhibition of plasma and RBC AChE (30–40%) observed at 4.72 mg/m^3 but not lower doses
- LD_{50}: 220 mg/kg (rats, dermal)
- NOAEL of 0.2-0.3 mg/kg/d for RBC AChE inhibition in dogs (repeated oral doses)

No evidence of carcinogenicity in humans, dogs, rats, or mice

No evidence of mutagenicity in *in vitro* and most *in vivo* assays.

DFG	***2019***	***MAK: 1 mg/m³***

MAK recommended to prevent adverse effects resulting from the inhibition of AChE.

Summary of additional data:

- NOAEC: 1.24 mg/m^3 (rats; 3 mo)
- Toxicokinetic conversions (using assumed inhalation absorption of 100%, bw 70 kg and respiratory volume of 10 m^3 for humans with consideration of species-specific correction value):
  - NOAEL: 0.75 mg/kg/d (rat; 2 yr feeding): ≡1.84 mg/m^3 in air

Source	Year set	Standard
		○ NOAEL: 0.98 mg/kg/d (mice; 2 yr feeding): ≡1.37 mg/m^3 in air ○ NOAEL: 0.16 mg/kg/d (dog; 1 yr oral): ≡1.12 mg/m^3 in air ○ NOAEL: 0.25 mg/kg/d (male human volunteers; 28 d oral): ≡1.75 mg/m^3 in air ○ NOAEL: 0.29 mg/kg/d (male human volunteers; 30 d oral): ≡2.03 mg/m^3 in air • MAK based on human studies above, deemed sufficiently low to prevent adverse effects • Neither genotoxic nor carcinogenic.
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
APVMA	✓	2006	• No additional information.
NICNAS	✓		• Not considered to pose an unreasonable risk to the health of workers and public health based on the Tier I human health risk assessment.

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, Sen
HCIS	Skin sensitisation – category 1
NICNAS	NA
EU Annex	Skin sensitisation – category 1
ECHA	—
ACGIH	Carcinogenicity – A4, DSEN, Skin
DFG	Sh (dermal sensitiser), H (skin)
SCOEL	NA
HCOTN	NA
IARC	—

Source	Notations
US NIOSH	SK:SYS, SK:SEN (draft)

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:	
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD_{50}/Inhalation LD_{50} <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:	317.32
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:	☐
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.

Australian Pesticides & Veterinary Medicines Authority (APVMA) (2006) Azinphos-methyl review – Preliminary Review Findings

Deutsche Forschungsgemeinschaft (DFG) (2019) Azinphos-methyl – MAK value documentation.

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).

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (Date unknown) Phosphorodithioic acid, O,O-dimethyl S-[(4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl] ester: Human health tier I assessment – IMAP report.

US National Institute for Occupational Safety and Health (NIOSH) (N.D.) NIOSH Skin Notation Profile Azinphos-methyl (draft)

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