PROPOXUR

CAS number: 114-26-1

Synonyms: Aprocarb, bay 39007, Baygon®, Blattanex®, IMPC, o-isoproxy-phenyl-N-methycarbamate, 2-isoproxyphenyl-N-methylcarbamate, PHC, Suncide®, Unden®

Chemical formula: $C_{11}H_{15}NO_3$

Structural formula: —

Workplace exposure standard (retained)

TWA: **0.5 mg/m³**

STEL: **—**

Peak limitation: **—**

Notations: **Sk.**

IDLH: **—**

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.5 mg/m³ is recommended to protect for cholinergic effects in exposed workers.

Discussion and conclusions

Propoxur is used as an insecticide.

The critical effect of exposure is cholinesterase (ChE) inhibition, which causes typical cholinergic symptoms.

A NOAEC of 3 mg/m³ for red blood cell (RBC) inhibition is reported in an acute volunteer inhalation study (ACGIH, 2018). Cholinergic symptoms were elicited in humans at an oral dose at 1.5 mg/kg and symptomless RBC ChE inhibition occurred at 1 mg/kg, which is equivalent to an air concentration of 7 mg/m³ over eight hours (ACGIH, 2018). Weak evidence for cholinergic symptoms resulting from putative dermal exposure is reported for exposed workers (ACGIH, 2018). A NOAEC of 18.7 mg/m³ for RBC, plasma and brain ChE inhibition is reported in a sub-chronic study in rats, whereas bladder carcinogenicity was observed at above 2.2 mg/m³ in a chronic exposure study in rats (ACGIH, 2018).

In view of the above information, the TWA of 0.5 mg/m³ is recommended to be retained, as derived by ACGIH (2018). The recommended TWA is expected to be protective of ChE inhibition and subsequent cholinergic effects and potential carcinogenicity observed in rats.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). The ACGIH (2018) recommendation for a carcinogenicity–A3 notation

is inconsistent with the current entry in the HCIS database. This evaluation did not find sufficient evidence for carcinogenicity in the remaining source material.

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

A skin notation is recommended due to evidence of dermal absorption and contribution to adverse systemic effects.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.5 mg/m^3***
ACGIH	***2016***	***TLV-TWA: 0.06 ppm (0.5 mg/m^3)***

TLV-TWA intended to protect for cholinergic effects resulting from ChE inhibition.

Summary of data:

TLV-TWA based on weight of human animal inhalation exposure data, which suggest a NOAEC range between 3–18.7 mg/m^3 for ChE inhibition; TLV-TWA of 0.5 mg/m^3 therefore sufficiently low.

A3 carcinogenicity notation recommended based on increased incidence of bladder papillomas and carcinomas in chronically fed rats.

Insufficient data to recommend a skin notation; agency notes dermal absorption is an important exposure route based on workplace data.

Human data:

- Cholinergic effects following acute poisoning subside within 24 h
- Cholinergic symptoms, likely from dermal exposure, in workers during spray applications
- No RBC ChE inhibition at 3 mg/m^3 in volunteer inhalation study (n=4, 4 h)
- RBC ChE activity at 27% of baseline and gastrointestinal disturbance from single oral dose of 1.5 mg/kg in volunteer study; no cholinergic effects:
  - RBC ChE activity 60% of baseline at 0.75 and 1 mg/kg ≡5.25 and 7 mg/m^3, respectively
- 16% of dermal dose systemically available when applied to forearm in volunteer study:
  - 18–64% of dermal dose excreted in another study
  - further study suggests dermal absorption increases with skin moisture and humidity
- Decreased birth length weakly correlated to propoxur exposure in prospective cohort study of pregnant women exposed to mixed pesticides (n=700, 1998–2002).

Animal data:

- LC_{50}: 654 mg/m^3 (rats, 4 h)
- Non-lethal in 3 dermal application studies at 500, 2,000 and 5,000 mg/kg (respectively chinchillas, rabbits, rats, 24 h):
  - muscle fasciculations reported in rabbits at 2,000 mg/kg
- NOAEL: 1,000 mg/kg (highest tested dose) for irritation, body weight changes, haematological and clinical chemistry changes:
  - ChE inhibition reported in sub-chronic dermal application study (rabbits, 6 h/d, 5 d/wk, 3 mo)
- RBC, plasma and brain ChE inhibition at 31.7 mg/m^3 in sub-chronic inhalation study with dose groups 5.7, 18.7 and 31.7 mg/m^3 (rats, 6 h/d, 5 d/wk, 12 wk)
  - NOAEC: 18.7 mg/m^3
- No histopathological evidence for carcinogenicity in chronic inhalation study with dose groups 2.2, 10.4, 50.5 mg/m^3 (rats, 6.3 h/d, 5 d/wk, 2 yr):
  - LOAEC: 10.4 mg/m^3 ≡0.6 mg/kg/d for ChE inhibition
  - NOAEC: 2.2 mg/m^3

Source	Year set	Standard
• Dose-related increased incidence of bladder tumours compared to controls in chronic feeding study with dose groups 10, 50, 250 mg/kg/d (rats, 2 yr): ○ NOAEL: 10 mg/kg/d • Dose-dependent chromosomal aberration in Chinese hamster ovarian cells *in vitro* • DNA damage *in vitro* using metabolic derivatives in human and mammalian cells • Micronucleus formation and chromosomal aberrations *in vivo* at ip dose of 25 mg/kg (mice). Insufficient data to recommend a sensitiser notation.		
DFG	***1979***	***MAK: 2 mg/m³***
Summary of additional information: Inadequate human data to derive MAK; sub-chronic inhalation experiment with rats indicates ChE inhibition threshold near 31.7 mg/m³ and NOAEC of 18.7 mg/m³ (also cited in ACGIH, 2018). Taken together with the low saturation point in air of 0.045 mg/m³, MAK of 2 mg/m³ expected to be protective of ChE inhibition and subsequent cholinergic symptoms. Human data: • Half-life ($t_{1/2}$): 8 h, 84% of IV doses excreted within 120 h. Animal data: • Non-mutagenic *in vivo* in dominant lethal test (mice, no further details provided). Insufficient data to assign notations for carcinogenicity, skin absorption, or sensitisation.		
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	• Tier I: agricultural use not assessed.
US EPA	✓	1987	• Oral reference dose (RfD) principally derived from volunteer single oral dose study, in which 43% inhibition of RBC ChE and mild cholinergic symptoms reported at 0.36 mg/kg; no NOAEL was experimentally determined • Inhalation RfD and carcinogenicity assessment not available.

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	—
NICNAS	—
EU Annex	—
ECHA	—
ACGIH	Carcinogenicity – A3
DFG	—
SCOEL	NA
HCOTN	NA
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:	no
Dermal repeat-dose NOAEL ≤200 mg/kg:	no
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?	No

Additional information

Molecular weight:	209.24
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 8.56 mg/m^3; 1 mg/m^3 = 0.12 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.

Deutsche Forschungsgemeinschaft (DFG) (1979) Propoxur – MAK value documentation, German language edition.

Deutsche Forschungsgemeinschaft (DFG) (2002) Propoxur – MAK value documentation, German language edition.

European Chemicals Agency (ECHA) (2020) Propoxur – REACH assessment.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) Phenol, 2-(1-methylethoxy)-, methylcarbamate: Human health tier I assessment – IMAP report.

US Environmental Protection Authority (US EPA) (1987) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Baygon.