HEPTACHLOR

CAS number:	76-44-8
Synonyms:	1,4,5,6,7,8,8a-Heptachloro-3a,4,7,7a-tetrahydro-4,7-methano-indene, 3-chloro-chlordene, heptagran, drinox H-34, heptamul, rhodiachlor, velsicol 104
Chemical formula:	$C_{10}H_5Cl_7$
Structural formula:	—

Workplace exposure standard (amended)

TWA:	**0.05 mg/m^3**
STEL:	—
Peak limitation:	—
Notations:	**Carc. 2, Sk.**
IDLH:	**35 mg/m^3**

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

Recommendation and basis for workplace exposure standard

A TWA of 0.05 mg/m^3 is recommended to protect for effects on the liver and the risk of cancer in exposed workers.

Discussion and conclusions

Heptachlor is as an insecticide that is well absorbed both orally and dermally and stored in the fatty tissue.

Critical effects associated with exposure are adverse liver effects. Effects on the blood and a possible link to cancer are observed. Heptachlor is not considered to be mutagenic (ACGIH, 2018).Several cases report an association between blood dyscrasias including leukaemia in humans and exposure to heptachlor (and chlordane), but no information on exposure levels are presented. A benchmark dose of 0.05 mg/kg/day was calculated from a two week feeding study in rats which corresponds to an airborne concentration of 0.1 mg/m^3 (DFG, 2008). A NOAEL of 0.025 mg/kg/day in dogs is reported in a two year feeding study, corresponding to a NOAEC of 0.15 mg/m^3 (DFG, 2008). Carcinomas of the liver are reported in mice fed 10 mg/kg/day over two years.

The TWA of 0.05 mg/m^3 published by ACGIH, (2018) and DFG, (2008) is recommended to be adopted and it is considered sufficiently protective for the critical effects identified in humans. DFG, (2008) derived the MAK by dividing the NOAEC of 0.15 mg/m^3 by a specific uncertainty factor.

Recommendation for notations

Classified as a category 2 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 based on evidence in animals.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.5 mg/m^3***
ACGIH	***2001***	***TLV-TWA: 0.05 mg/m^3***

TLV-TWA is recommended to protect for liver damage as reported in animals and to minimise the potential for blood dyscrasias and possible cancer.

Summary of data:

Human data:

- Several case reports describing the association between blood dyscrasias including leukaemia in humans and exposure to heptachlor (and chlordane); no information on exposure levels
- No dose-dependent relationship between exposure and aplastic anaemia.

Animal data:

- Dermal LD_{50} range: 119–2,000 mg/kg in rats, rabbits, and guinea pigs
- LC_{50}: 150 mg/m^3 (cats, 4 h)
- Rats fed 7–12 mg/kg/d for 14 d and 10 mg/kg/d for 5–7 d showed significant liver damage and altered liver function
- Rats treated intramuscularly with daily doses of 3 or 15 mg/kg/d; significant decrease in liver weight; significant decrease in testes weight at 15 mg/kg/d
- Pigs dosed daily with 2 or 5 mg/kg for 78 d; ultrastructural changes in liver
- NOEL of 5 mg/kg/d in rats; regenerative liver changes; 2 yr feeding study
- Carcinomas of the liver observed in mice fed 10 mg/kg/d over 2 yr.

Low mutagenic activity.

TLV-TWA justified by results of long-term studies; no derivation offered.

Skin notation warranted.

Insufficient data to recommend a sensitiser notation or STEL.

DFG	***2008***	***MAK: 0.05 mg/m^3***

Summary of additional data:

- Critical effect is enzyme induction in the liver
- BMDL of 0.05 mg/kg/d for enzyme induction calculated from a 2 wk feeding study on rats; toxicokinetic transmission to airborne concentration of 0.1 mg/m^3 using following factors:
  - 7/5 conversion for daily animal exposure to workweek exposure
  - 1:4 rat-human species-specific correction value; as per DFG methodology
  - oral absorption of 84% in rats
  - 70 kg worker inhaling 10 m^3 per 8 h shift
  - inhaled concentration = (oral dose x oral absorption in animal x 70 kg bw)/ (species-specific correction value x inhalation absorption in humans x 10^3/d)

Source	Year set	Standard
• NOAEL of 0.025 mg/kg/d in dogs for histopathological or biochemical changes; 2 yr feeding study; toxicokinetic transmission to airborne concentration of 0.15 mg/m^3 using following factors: ○ 7/5 conversion for daily animal exposure to workweek exposure ○ 1:1.4 dog-human species-specific correction value; as per DFG methodology ○ oral absorption of 84% in rats ○ 70 kg worker inhaling 10 m^3 per 8 h shift ○ inhaled concentration = (oral dose x oral absorption in animal x 70 kg bw)/ (species-specific correction value x inhalation absorption in humans x 10^3/d) • Converted PODs are in the same range for 2 species justifies MAK of 0.05 mg/m^3.		
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
US EPA	✓	1987	• NOEL of 0.15 mg/kg in rats; liver weight increases in males; 2 yr feeding study.

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	Carc. 2, Skin
HCIS	Carcinogenicity – category 2
NICNAS	NA
EU Annex	Carcinogenicity – category 2
ECHA	Carc. 2
ACGIH	Carcinogenicity – A3, Skin
DFG	Carcinogenicity – 4, H (skin)
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 2B
US NIOSH	SK:SYS

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:	
Dermal LD_{50} ≤1000 mg/kg:	yes
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%:	
	consider assigning a skin notation

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	373.32
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 15.93 mg/m^3; 1 mg/m^3 = 0.06 ppm
This chemical is used as a pesticide:	✓
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐

Molecular weight:	373.32
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 15.93 mg/m^3; 1 mg/m^3 = 0.06 ppm
This chemical is used as a pesticide:	✓
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) (2012) Heptachlor – 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).

International Agency for Research on Cancer (IARC) (2001) Heptachlor. IARC Monographs on the evaluation of the carcinogenic risk to humans.

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

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

US National Institute for Occupational Safety and Health (NIOSH) (2017) NIOSH Skin Notation Profiles: Heptachlor.