PENTACHLORONITROBENZENE

CAS number: 82-68-8

Synonyms: Avicol, botrikex, brassicol, folosan, PCNB, quintozene, terraclor

Chemical formula: $C_6Cl_5NO_2$

Structural formula: —

Workplace exposure standard (retained)

TWA: **0.5 mg/m^3**

STEL: **—**

Peak limitation: **—**

Notations: **DSEN**

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/m^3 is recommended to protect for adverse liver effects and skin sensitisation in exposed workers.

Discussion and conclusions

Pentachloronitrobenzene (PCNB) is used as a fungicide.

Critical effects of exposure are liver damage and skin sensitisation.

Human exposure data are limited and indicate dermal sensitisation potential in a volunteer patch test study (ACGIH, 2018). Carcinogenicity reported in chronic feeding and dermal application studies in mice is associated with hexachlorobenzene (HCB) impurities in technical grade mixtures (ACGIH, 2018). A systemic NOAEL of 0.75 mg/kg/day and corresponding LOAEL of 4.5 mg/kg/day for reversible liver and bile production effects are reported in a chronic feeding study with dogs (ACGIH, 2018).

In the absence of suitable human exposure data, the TWA of 0.5 mg/m^3 by ACGIH, (2018) is recommended to be retained to protect for liver effects and skin sensitisation in exposed workers. In accordance with the evaluation by ACGIH, (2018), the TWA is derived from the oral NOAEL and LOAEL for systemic effects in dogs by extrapolating to equivalent inhalational NOAEC of 5.25 mg/m^3 and LOAEC of 31.5 mg/m^3, respectively (ACGIH, 2018). The margin of safety from the estimated NOAEC to the recommended TWA is considered sufficiently large to be protective of the critical effects.

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.

There are insufficient data to recommend a skin notation. However, it is recommended that a further review be undertaken given that dermal sensitisation occurs which is suggestive of systemic effects.

APPENDIX

Primary sources with reports

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

TLV-TWA intended to minimise potential for adverse liver effects and possible skin sensitisation.

Not considered carcinogenic in humans (A4); positive results in chronic animal study due to hexachlorobenzene (HCB) impurities present in technical grade mixture. US EPA recommends a reduction in HCB contamination to 0.1% in technical grade mixtures.

Summary of data:

TLV-TWA expected to be protective of systemic liver effects observed in dogs and derived from NOAEL of 0.75 mg/kg/d in chronic feeding study; inhalational equivalent dose is 5.25 mg/m^3 assuming 10 m^3 respiratory volume of 8 h shift for 70-kg worker.

Human data:

- Sensitisation in 13/50 volunteers after second application in patch test using 75% wettable powder (no further details)
- one case of reversible corneal inflammation from accidental spill into eyes.

Animal data:

- LD_{50}: >4,000 mg/kg (rabbits, dermal); 14 d observation period, no evidence for toxicity
- Liver hypertrophy and growth depression reported in sub-chronic controlled feeding study with dose range 63.5–5,000 ppm in diet using technical grade PCNB (young rats, 3 mo):
  - liver hypertrophy observed in all dose groups except at 63.5 ppm in diet in females
  - growth depression observed at 5,000 ppm (females) and 2,500 ppm (males)
- Increased incidence of liver tumours in males in controlled chronic gavage/feeding study:
  - average exposure at 169 mg/kg/d technical grade PCNB with ≤11% HCB (mice, 82 wk)
- Exposure-related incidence of subcutaneous tumours at 1,200 ppm in female mice in controlled chronic feeding study using technical grade PCNB with 2.7% HCB (mice, rats, 2 yr):
  - no tumours reported in male or female rats or male mice
- No abnormal or significantly increased tumorigenicity at 5,417/7,875 and 10,064/14,635 ppm in diet (male/female rats) or 5,213/8,187 and 2,606/4,093 ppm in diet (male/female mice) using 97% PCNB containing 1% HCB in 78 wk controlled feeding study:
  - low survival in male mice (including controls)
  - similar results in US NTP carcinogenicity study with dose groups 0, 2,500 and 5,000 ppm in diet (mice, duration not specified, presumed 2 yr)
- Reversible, dose-dependent adverse liver effects (cholestasis) and bile nephrosis at 180 ppm in diet in chronic feeding study, dose groups 0, 5, 30, 180, 1,080 ppm in diet (dogs, 2 yr):
  - NOAEL: 30 ppm in diet ≡0.75 mg/kg/d, LOAEL: 180 ppm in diet:
  - changes in clinical blood biochemistry at 1,080 ppm in diet
- 87% PCNB contaminated with HCB was teratogenic, 99% PCNB not teratogenic at 500 mg/kg/d (mice, GD 7–11)

Source	Year set	Standard
• Negative mutagenicity *in vitro* in bacteria and mouse lymphoma cells and *in vivo* in mice and *D. melanogaster*; clastogenic *in vitro* in Chinese hamster ovarian cells. Insufficient data to recommend a TLV-STEL or notations for skin absorption or sensitisation.		
DFG	***NA***	***NA***
No report.		
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
IARC	✓	1974	• Minimum purity of technical grade PCNB in US is 99% • Increased incidence of skin tumours in dermal application study using 0.2 mL of 0.3% solution in croton oil (12 wk) then acetone (20 wk); 12 tumours in 9 control survivors versus 50 tumours in 13 dosed survivors (mice, n=20, 32 wk): o study not considered in evaluation due to inadequate controls • 62% of oral dose of 2,000 mg excreted unchanged, 26% excreted as metabolites • Low potential for accumulation based on chronic feeding studies with rats fed 500 ppm in diet and dogs fed 1,080 ppm in diet.
US EPA	✓	1987	• 2 yr chronic feeding study with dogs (also cited in ACGIH, 2018) used as principal study to derive oral reference dose (RfD); NOAEL: 0.75 mg/kg/d, LOAEL: 4.5 mg/kg/d.

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	Sen
HCIS	Skin sensitisation – category 1

Source	Notations
NICNAS	—
EU Annex	Skin sensitisation – category 1
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	NA
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
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:	
Dermal LD_{50} ≤1000 mg/kg:	no
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 not warranted

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	295.36
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:	☐
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.

International Agency for Research on Cancer (IARC) (1974) Volume 5, Some organochlorine pesticides. 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 – Pentachloronitrobenzene (PCNB).