HEXACHLOROBUTADIENE

CAS number: 87-68-3

Synonyms: HCBD, hexachloro-1,3-butadiene

Chemical formula: C_4Cl_6

Structural formula: —

Workplace exposure standard (retained)

TWA: **0.02 ppm (0.21 mg/m^3)**

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 0.02 ppm (0.21 mg/m^3) is recommended to protect for kidney damage and eye and upper respiratory irritation in exposed workers.

Discussion and conclusions

Hexachlorobutadiene (HCBD) is a by-product of processes associated with the chlorination of hydrocarbons and has been used as a solvent for elastomers, heat transfer liquid, transformer and hydraulic fluid. HCBD has also been used as a pesticide with limited applications.

No human data are available. In animals, critical effects include kidney damage, carcinogenicity and possible irritation (ACGIH, 2018).

A two year feeding study in rats identified a NOAEL of 0.2 mg/kg/day for adverse kidney effects. Both ACGIH (2018) and DFG (2015) use this NOAEL as a starting point to calculate a TWA of 0.02 ppm (0.21 mg/m^3) by different methods. The TWA of 0.02 ppm is retained and considered protective of kidney damage and irritation effects in exposed workers.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). There is evidence of carcinogenicity in rats with unknown relevance to humans. A review of the carcinogenicity classification is recommended.

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: 0.02 ppm (0.21 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 0.02 ppm (0.21 mg/m^3)***

TLV-TWA recommended to minimise potential for kidney damage and provide a wide margin of protection against eye and upper respiratory irritation.

Summary of data:

NOAEL of 0.2 mg/kg/d corresponds to an equivalent TWA exposure of 1.4 mg/m^3 (1.3 ppm) based on a 70 kg worker inhaling 10 m^3 of air over an 8 h shift assuming 100% absorption.

ACGIH recommend TLV-TWA of 0.02 ppm on this basis without further explanation.

Human data:

- No human data presented.

Animal data:

- LD_{50}: 90 mg/kg for guinea pigs; 87–116 mg/kg for mice; 200–350 mg/kg for rats
- Absorbed through skin of rabbits; dosage causing death by dermal absorption are in the same range as by oral administration
- No adverse effects reported from short-term repeated inhalation studies in mice and rats repeatedly exposed at 24 mg/m^3 (2.3 ppm) for 7 mo; no further information
- NOAEL of 0.2 mg/kg/d for kidney damage reported in rats; 2 yr feeding study
- Lifetime carcinogenic feeding response study in rats:
    - increased mortality (males), decreased body weight gain (males and females), urinary excretion of coproporphyrin (males and females) at highest dose 20 mg/kg/d
    - increased hyperplasia and neoplasia of renal tubular epithelium, neoplastic nodules in the kidneys shown to be adenomas or adenocarcinomas at 20 mg/kg/d
    - increased urinary excretion of coproporphyrin (females only) and hyperplasia of renal tubular epithelium but no neoplasms at 2 mg/kg/d
    - no adverse effects at 0.2 mg/kg/d
    - concluded dose-response effect on kidney with renal neoplasms only at a dose level higher than causing renal damage; A3 carcinogenicity notation applied.

Genotoxicity data:

- Negative in the *Salmonella* assay
- Negative in *Drosophila* test for sex-linked recessive lethal mutations
- Negative for the induction of chromosomal aberrations in cultured Chinese hamster ovary cells.

DFG	***2015***	***MAK: 0.02 ppm (0.22 mg/m^3)***

Summary of additional data:

- Insufficient human data to derive MAK
- Irritating to the eyes, nose and respiratory tract in rats at 25 ppm; respiratory distress 100 ppm; sub-chronic repeated inhalation exposure

Source	Year set	Standard

• NOAEL of 0.2 mg/kg/d in rats for body weight and kidney effect; 2 yr feeding study
• Lowest dose of 0.2 mg/kg/d in mice caused renal toxicity in 13 wk feeding study; calculated BMDL of 0.1 mg/kg/d
• Metabolic similarities between rats and humans (compared to mice) warrant use of rat NOAEL over mice
• Transfer of NOAEL of 0.2 mg/kg/d:
  ○ 7/5 to account for animal daily exposure compared to 5 d work week
  ○ 1:4 species-specific correction factor; toxicokinetic difference between rats and humans
  ○ assumed oral absorption (100%), body weight (70 kg) and respiratory volume (10 m^3)
  ○ extrapolated to an equivalent inhalation exposure of 0.49 mg/m^3 (0.045 ppm); divided by 2 according to DFG methodology
  ○ MAK 0.02 ppm (0.22 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
IARC	✓	1999	• Weak evidence for genotoxicity in mammalian cells *in vitro* • Mutagenicity results in bacteria are unclear.
NTP	✓	2000	• Observations of mutagenicity in bacteria under conditions that favour the GSH/mercapturate/b-lyase pathway • Genotoxicity in mammalian cells • Genotoxicity *in vivo* DNA binding in rats and mice.

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	Skin
HCIS	NA

Source	Notations
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A3, Skin
DFG	Carcinogenicity – 4, H (skin)
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:	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? No

Additional information

Molecular weight:	260.76
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 10.67 mg/m^3; 1 mg/m^3 = 0.094 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) (2016) Hexachlorbutadien – MAK value documentation.

International Agency for Research on Cancer (IARC) (1999) Hexachlorobutadiene. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Toxicology Program (NTP) (2000) NTP-RoC: Hexachlorobutadiene.