# Hexachlorobutadiene

| CAS number: | 87-68-3 |
| --- | --- |
| Synonyms: | HCBD, hexachloro-1,3-butadiene |
| Chemical formula: | C4Cl6 |
| Structural formula: | — |

 Workplace exposure standard (retained)

| TWA: | **0.02 ppm (0.21 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 0.02 ppm (0.21 mg/m3) 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/m3) 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/m3) |
|  |
| ACGIH 2001 TLV-TWA: 0.02 ppm (0.21 mg/m3) |
| 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/m3 (1.3 ppm) based on a 70 kg worker inhaling 10 m3 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:* LD50:90 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/m3 (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/m3) |
| 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
* 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 m3)
* extrapolated to an equivalent inhalation exposure of 0.49 mg/m3 (0.045 ppm); divided by 2 according to DFG methodology
* MAK 0.02 ppm (0.22 mg/m3).
 |
| 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 |
| 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 LD50 ≤1000 mg/kg: | yes | 3.00 |   |
| Dermal repeat-dose NOAEL ≤200 mg/kg: |   |   |   |
| Dermal LD50/Inhalation LD50 <10: |   |   |   |
| *In vivo* dermal absorption rate >10%: |   |   |   |
| Estimated dermal exposure at WES >10%: |   |   |   |
|   |   | 3 | **consider assigning a skin notation** |

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### 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/m3; 1 mg/m3 = 0.094 ppm |
| This chemical is used as a pesticide: |[x]
| This chemical is a biological product: |[ ]
| This chemical is a by-product of a process: |[x]
| 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*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) 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.