# Chlorinated diphenyl oxide

| CAS number: | 31242-93-0 |
| --- | --- |
| Synonyms: | Chlorinated phenyl ether, hexachlorobiphenyl oxide |
| Chemical formula: | C12H4Cl6O (average) |
| Structural formula: | — |

Workplace exposure standard (retained)

| TWA: | **0.5 mg/m3** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **—** |
| 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 liver damage and acneiform dermatitis in exposed workers.

## Discussion and conclusions

Chlorinated diphenyl oxides are encountered as intermediates in chemical manufacture, corrosion inhibitors, dry-cleaning detergents, thermal lubricants, and as additives for soaps and lotions.

A total of 209 chlorinated diphenyl oxide derivatives exist and generally have common toxic endpoints. The degree of chlorination has a positive relationship to the severity of toxic effects and retention in adipose tissue following absorption (HCOTN, 2003). Chronic exposure and carcinogenicity studies are limited. However, some compounds are demonstrably non-mutagenic *in vitro* (HCOTN, 2003). Critical effects of exposure include hepatotoxicity and acneiform dermatitis; prolonged contact may cause severe itching. ACGIH (2018) recommends an occupational exposure level of 0.5 mg/m3 to protect for hepatotoxicity based on a chronic, inhalational, rat study (supported by a four-week feeding study in rabbits).

In the absence of additional data the current TWA of 0.5 mg/m3 is retained. The recommended TWA is considered protective for hepatotoxicity and acneiform dermatitis.

## Recommendation for notations

Not classified as a 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 not recommended based on the available data. Although systemic toxicity is reported in a repeat dermal exposure study in rabbits, the available data is considered insufficient to support a skin notation, (HCOTN, 2003).

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1995 TWA: 0.5 mg/m3 | |
|  |
| ACGIH 2001 TLV–TWA: 0.5 mg/m3 |
| TLV–TWA intended to protect for hepatotoxicity and acneiform dermatitis. Insufficient data available to recommend a TLV-STEL or notations for skin absorption, sensitisation, or carcinogenicity. TLV‑STEL of 2 mg/m3 withdrawn in 1990.  Summary of data:  TLV-TWA is based on a cited recommendation of 0.5 mg/m3 reported in a repeat inhalation study with rats and a 4 wk oral dose study with rabbits that reported NOAELs between 0.1–1 mg/kg/d. Liver toxicity was the endpoint in both studies.  Toxicological studies of tetra-, penta-, and hexachloro diphenyl ethers are discussed in tandem for the purposes of the agency’s assessment.  Mutagenicity and carcinogenicity are not discussed.  Human data:   * Toxicity in humans characterised as acneiform dermatitis and/or systemic intoxication * Prolonged skin contact causes acneiform dermatitis at the contact site and may cause intense itching * Systemic toxicity not reported in exposed workers.   Animal data:   * LD50: 50–100 mg/kg (guinea pigs); for tetra-, penta-, hexachloro derivatives * Penta- and hexachloro derivatives cause severe skin irritation in rabbits (no further information provided) * Repeat oral dose studies with either penta- or hexachloro derivative reported liver toxicity (rabbits, dose frequencies not specified, 4 wk); hexachloro derivative is more acutely toxic   + Pentachloro derivative NOAEL of 1 mg/kg/d for liver injury; LOAEL of 10 mg/kg/d; moderate liver injury and no growth reported at 100 mg/kg   + Hexachloro derivative NOAEL of 0.1 mg/kg/d for liver injury; LOAEL of 1 mg/kg/d for severe liver injury; death occurred at 5 mg/kg. * Congestion and fatty degeneration of liver reported in chronic inhalational study using mixtures of chlorinated diphenyl oxides with a chlorine content of 54–57% (rats, 134 d). Although doses and exposure duration are not mentioned, cited report recommends 0.5 mg/m3 as a permissible concentration for the workplace. |
| DFG NA NA |
| No report. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2003 8-hour TWA: 0.5 mg/m3 |
| Summary of additional data:  Available data inadequate to recommend health-based TWA.  No data on skin sensitisation, chronic toxicity, or carcinogenicity.  There are 209 possible congeners and isomers   * log KOW: 4.45–8.16 mg/L * aqueous solubility: 0.06 ng/L to 12.7 mg/L.   Human data:   * Chlorinated diphenyl ethers in adipose tissue of a Canadian population at mean values of 1.53 and 0.38 ng/g of nonachlorodiphenyl oxide and decachlorodiphenyl oxide, respectively.   Animal data:   * LD50: 600–1200 and 50–100 mg/kg (guinea pigs, oral); for mono- to trichloro diphenyl oxide and tetra- to pentachloro diphenyl oxide, respectively * LD50: 50 mg/kg (guinea pigs, oral) for hexachloro congener * ED50 for immunosuppression parameters determined for a range of polychlorinated congeners (mice, single IP)   + ED50 range: 0.17 to >151 mg/kg   + potency depends on position and number of chlorine substituents * Rats exposed *via* IV with a pentachloro derivative showed substance accumulation in skin (after 1 d) and adipose tissue (after 4 d)   + unreacted substance remained in adipose tissue 21 d after injection   + half-life in blood estimated 5.8 d * Chloracne, gross and microscopic liver damage, microscopic damage to kidneys and spleen reported in repeat dermal exposure study with 0.2 mL of hexachloro derivative (rabbits, n=4, 10% in olive oil, 1 time/wk, 4 wk)   + adverse effects presented after 3 wk   + 2 animals died following treatment * Repeat feeding studies with penta-, hexa-, and heptachloro diphenyl oxides generally showed mild histological changes to liver and thyroid at high doses (rats, n=10/sex/congener, by gavage or in diet, 28 d)   + male rats were more sensitive to dietary route than females   + NOAEL of 4 mg/kg/d; LOAEL of 40 mg/kg/d when administered by gavage; for all congeners   + NOAEL of 0.7 and 6.1 mg/kg/d (males and females, respectively); pentachloro derivative * Available developmental toxicity data inconclusive * 2 tested tetrachloro isomers not mutagenic in bacteria. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| US NIOSH |  | 1994 | * No inhalation toxicity data available from which to derive an IDLH * Previous value of 35 mg/m3 based on acute oral toxicity data in animals * Revised IDLH of 5 mg/m3 is based on 10-fold factor of the NIOSH REL and OSHA PEL of 0.5 mg/m3. |

### 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 | — |
| HCIS | NA |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | — |
| DFG | NA |
| SCOEL | NA |
| HCOTN | — |
| 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 |
| --- |
| Insufficient data to warrant a skin notation. |

### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

| Molecular weight: | 204.7 to 514.7 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = Number mg/m3; 1 mg/m3 = 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*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

Health Council of the Netherlands (HCOTN) (2003) Chlorinated diphenyl oxides. Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/078.

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