# 2,6-Di-tert-butyl-p-cresol

| CAS number: | 128-37-0 |
| --- | --- |
| Synonyms: | BHT, DBPD, 2,6-bis(1,1-Dimethylethyl)-4-methylphenol, butylated hydroxytoluene |
| Chemical formula: | C15H24O |
| Structural formula: | — |

Workplace exposure standard (interim)

| TWA: | **10 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

An interim TWA of 10 mg/m3 is recommended to protect for adverse effects on the liver in exposed workers.

Given the limited data available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

## Discussion and conclusions

2,6-Di-tert-butyl-*p*-cresol (BHT) is used in ground vehicle and aviation fuels, lubricants, turbines and insulating oils. BHT is also used as a food antioxidant and in food packaging materials.

Critical effects of exposure include respiratory irritation and effects of the liver. Limited human toxicological data are available. The ACGIH (2018) reports a calculated exposure concentration that produces a 50% respiratory rate decrease (RD50) of 3.6 ppm (32.4 mg/m3) in male mice and uses this figure as part of an unconvincing basis to assign a TWA of 2 mg/m3. A NOAEL of 10 mg/kg/day in rats for increased relative liver weight and increased liver enzyme activity is reported in a 22-month feeding study. Based on generic factors this oral dose is equivalent to human NOAEC of 22 mg/m3 (DFG, 2012). A two-generation reproductive study reported a NOAEL of 25 mg/kg/day in rats for decreased body weight in offspring and induction of liver enzymes (HCOTN, 2004).

A TWA of 10 mg/m3, as assigned by SWA, DFG (2012) and HCTON (2004) is recommended in the interim to protect for liver effects. As there are limited data indicating sensory irritation and some residual uncertainties regarding its significance to humans, it is recommended that an investigation of additional data sources is undertaken at the next scheduled review.

## 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. Skin sensitisation and allergic effects reported in primary sources. A review of the classification for skin sensitisation is recommended.

A skin notation is recommended based on case study suggesting potential dermal absorption and sensitisation effects in humans.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 10 mg/m3 | |
|  |
| ACGIH 2001 TLV-TWA: 2 mg/m3 |
| TLV-TWA recommended to reduce the risk of sensory irritation.  Summary of data:  Low vapour pressure; non-volatile solid; saturated vapour concentration of ~120 mg/m3  Human data:   * Limited data available * WHO ADI 0.5 mg/kg/d; human dietary intake in USA estimated at 0.2 mg/kg/d * Effects thought to be allergen based; patients suspected of BHT sensitivity responded with exacerbation of vasomotor rhinitis, headaches, flushing and on occasion, a flare-up of asthma and other symptoms when challenged with doses of 100 and 250 mg; no further information * No sensitising action documented in a study of 1336 patients; authors concluded that when used as an antioxidant, normal use concentrations can be regarded safe in relation to allergic contact dermatitis; no further information   Animal data:   * Acute, subacute and chronic toxicity has been comprehensively reviewed *via* oral or intraperitoneal dosing; limited data *via* inhalation route likely due to low vapour pressure * In a study of potential irritant effects of chemicals emitted from carpets, the authors reported a calculated RD50 (respiratory rate decrease) of 3.6 ppm (95% Cl:2.1–36) in male mice * based on published information regarding the correlationof RD50 data and human responses to sensory irritants. A concentration of 0.1 x RD50 (0.36 ppm or 3.24 mg/m3) may produce slight but tolerable irritation * No histopathological changes in 12 mo oral study in dogs * No histopathological changes in 24 mo oral study in rats.   No clear derivation of the TLV is provided; TLV-TWA of 2 mg/m3 is based on the following:   * The ACGIH report that results of respiratory depression bioassays can be used to suggest OEL for respiratory irritants; OELs are often derived *via* the calculation 0.03 x RD and deemed as acceptable; no further information * A concentration of 0.1 x RD50 (0.36 ppm or 3.24 mg/m3) may produce slight but tolerable irritation; based on published information regarding the correlation of RD50 data and human responses to sensory irritants * No evidence of respiratory or sensory irritation has been reported in the available literature in workers since the TLV of 10 mg/m3 was established in 1976. |
| DFG 2012 MAK: 10 mg/m3 |
| Summary of additional data:   * NOEL of 10 mg/kg/d in rats; increases in liver relative weight and liver enzyme activity at higher concentrations; 22 mo feeding study * MAK of 10 mg/m3 (rounded) derived using no effect level and following factors: * adjustment for daily exposure in animals to 5 d work week 7/5 * species correction factor of 1:4 * oral absorption of 90% in rats * 70 kg worker inhaling 10 m3 in 8 h * ≡22 mg/m3: divided by an uncertainty factor of 2 for using an oral study resulting in a TWA of 10 mg/m3. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2004 TWA: 10 mg/m3 |
| Current TWA is an administrative OEL.  A health-based TWA of 5 mg/m3 is recommended based on the following information.  Summary of additional data:   * Case studies suggest mildly irritating to skin; skin sensitiser in some cases (humans) * Slightly irritating to the skin and the eyes of rabbits * No skin sensitisation was demonstrated in guinea pigs * NOAEL of 25 mg/kg/d in rats; decrease in body weight in BHT-treated offspring and hepatic enzyme induction; 2-gen reproductive study * TWA of 5 mg/m3 (rounded) derived using NOAEL and following factors: * adjustment for daily exposure in animals to 5 d work week 7/5 * allometric scaling of rats to humans =4 * overall factor of 18 (explanation not included), covering inter- and intraspecies variation * 70 kg worker inhaling 10 m3 in 8 h. |

### Secondary source reports relied upon

NIL.

### 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 | Carcinogenicity – A4 |
| DFG | Carcinogenicity – 4 |
| SCOEL | NA |
| HCOTN | — |
| IARC | Carcinogenicity – category 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: | yes | 4.00 |  | | Dermal LD50 ≤1000 mg/kg: |  |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  |  | **a skin notation is warranted** | |

### IDLH

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

## Additional information

| Molecular weight: | 220.35 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 9.01 mg/m3; 1 mg/m3 = 0.11 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.

Deutsche Forschungsgemeinschaft (DFG) (2012) 2,6-Di-tert-butyl-p-cresol (BHT) – MAK value documentation.

Health Council of the Netherlands (HCOTN) (2004) 2,6-Di-tert-butyl-p-cresol. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/101.

International Agency for Research on Cancer (IARC) (1987) Butylated hydroxytoluene (BHT). IARC Monographs on the evaluation of the carcinogenic risk to humans.