# tert-butyl alcohol

| CAS number: | 75-65-0 |
| --- | --- |
| Synonyms: | t-butanol, tertiary-butanol, 2-methyl-2-propanol,  trimethylcarbinol |
| Chemical formula: | C4H10O |
| Structural formula: |  |

Workplace exposure standard (amended)

| TWA: | **20 ppm (62 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **1,600 ppm** |
| Sampling and analysis: | The recommended value is readily quantifiable through currently available sampling and analysis techniques. |

## Recommendation and basis for workplace exposure standard

A TWA of 20 ppm (62 mg/m3) is recommended to protect for kidney damage and potential narcosis in exposed workers. The previous STEL of 150 ppm (455 mg/m3) is recommended to be withdrawn as there is a lack of evidence for immediate acute toxicity within ten times of the recommended TWA.

## Discussion and conclusions

tert-Butyl alcohol is used in industrial synthesis, as a dehydrating agent, as a chemical intermediate and solvent in pharmaceutical manufacture, denaturant for ethanol and antiknock agent.

Unlike related unbranched primary alcohols, the evidence for irritation effects following exposure are equivocal in humans and animals. The critical effect of exposure is considered to be nephrotoxicity with the potential for narcosis at higher concentrations. Reports in animals of narcotic effects at exposures above those which cause nephrotoxicity have not been affirmed in human exposure data (ACGIH, 2018; DFG, 2003). Very limited substance-specific human exposure data suggest that nasal irritation occurs at high concentrations relative to those that cause nephrotoxic effects in animals (DFG, 2003).

The TWA of 20 ppm (62 mg/m3) is adopted from the DFG recommendation. This value is derived from a LOEL of 135 ppm for nephrotoxicity from a well-conducted chronic inhalation study in rats. The LOEL in this study is presumed to be close to a NOAEL due to the weak toxic effects observed at this concentration (DFG, 2003). At the recommended TWA, a 70 kilogram worker with an inhalation rate of 10 m3 per eight hour shift will inhale a maximum dose of approximately 10 mg/kg. The recommended TWA is considered sufficiently protective of nephrotoxic effects seen in male rats (DFG, 2003). As there is insufficient data to suggest an immediately acute effect at concentrations within ten times of the recommended TWA, the previous STEL of 150 ppm is recommended to be withdrawn.

## 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 as there is no evidence of systemic effects resulting from skin absorption.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA Year TWA: 100 ppm (303 mg/m3); STEL: 150 ppm (455 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 100 ppm (303 mg/m3) |
| TLV-TWA recommended to minimise the risk of narcosis.  Summary of data:  TLV-TWA intended to minimise potential for narcosis. Its derivation is unclear from the discussed studies, but weight of evidence from animal studies suggests that observance of the TLV-TWA will protect for critical effects such as narcosis and changes to kidney and liver function.  Physical dependence and withdrawal symptoms noted in animal studies have not been affirmed in any available human data.  Insufficient data to assign a STEL or notations for skin absorption or sensitisation.  Not classifiable as a human carcinogen due to equivocal animal data (A4).  Human data:   * Slight erythema and hyperaemia when applied to skin of volunteers (n=5) * failed to elicit allergic response in subjects with ethanol allergy * Allergic contact dermatitis reported for sunscreen containing tert‑butanol.   Animal data:   * LD50: 3,500 mg/kg (rats, oral), 3,557 mg/kg (rabbits, oral); * Narcotic dose: 1,480 mg/kg (rabbits, oral) * Severe narcosis and death at 10,000 ppm (rats, 7 h) * Elimination half-times in blood: 4–9 h (rats, guinea pigs) * Very high concentrations (not specified) did not cause irritation to eyes, upper respiratory tract or mucous membranes in rodents * Hypothermia and reduced body weight reported in repeat ip injection study at   0.2–0.8 mg/kg (rats and guinea pigs, every 8 h, 4 d)   * cessation caused withdrawal syndromes e.g. convulsions * similar results obtained from repeat feeding study with rats and behavioural disorders noted in mice during withdrawal * Physical dependence 4–5 times more potent than ethanol based repeat dose study with mice at 500–750 mg/kg (single ip) followed by >3,700 ppm (continuous, 1–9 d) * after 3–5 h, withdrawal caused tremor, hyperexcitability, convulsions sometimes causing death, tolerance rapidly formed based on elimination rates decreasing from   8–9 h to <3 h after 3 d   * Changes to liver fatty acid metabolism after single oral dose of 1,850 mg/kg or inhalation of 500 ppm (5 d) or 2,000 ppm (3 d) ppm (rats) * MTD of 1% w/v≡7,000 mg/kg/d in repeat feeding study (mice, 15 d) * Skin tumour produced with 16.6% benzene solution in chronic dermal application study (mice, n=50, 150 d) * Evidence of carcinogenicity in male rats and female mice reported from chronic feeding study: 90–650 mg/kg/d (rats; 2 yr), 510–2,110 mg/kg/d (mice, 2 yr) * Dose-dependent maternal body weight gain and foetal body weight reduction in developmental study * treatment range: 3–7 mg/kg/d (mice, day 6–20 of gestation) * concluded tert-butanol 4–5 times more potent than ethanol in causing congenital behavioural defects * Non-mutagenic *in vitro*; protects single and double stranded DNA and L5178Y mouse lymphoma cells against mutagenic/clastogenic effects of ionising radiation. |
| DFG 1999 MAK: 20 ppm (62 mg/m3) |
| MAK value recommended to protect for nephrotoxicity.  Summary of additional data:  Previous MAK of 100 ppm withdrawn due to evidence of nephrotoxicity at 135 ppm in male rats reported in a chronic inhalation study  Current MAK based on NOAEL estimated by the LOEL from this study.  Assuming a respiratory volume of 10 m3, a 70 kg worker would have a maximum daily dose of 10 mg/kg if the MAK is observed; 8 times lower than the equivalent dose received at the LOEL for renal toxicity  Insufficient evidence to warrant a skin or sensitisation notation.  Human data:   * Nasal irritation threshold: 32,809 ppm (2 s) with anosmic volunteers.   Animal data:   * LD50:>2,000 mg/kg (rabbits, dermal) * Repeat inhalation exposure study 135–2,100 ppm generally found no histopathological changes except for increased kidney and liver weights (mice and rats, 6 h/d, 5 d/wk, 90 d) * LOEL of 135 ppm for spontaneous nephropathy in male rats (presumed to be close to the NOAEL, as observed toxicity was minor) * NOEL <250 mg/kg/d (male rats), 770 mg/kg/d (female rats) for ataxia (oral, 90 d) * Human relevance of increased thyroid tumour incidence in chronic feeding study with rats questioned because tumours occurred in only one sec and above the maximum tolerated dose * Contradictory sensitisation results from standardised maximisation test (guinea pigs), which report either weak or no potential for skin sensitisation. |
| 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 |
| --- | --- | --- | --- |
| NICNAS |  | 2013 | * Vapours reported as irritating to eyes, nose and throat in humans (concentrations not specified) * Modes of renal carcinogenicity in rats have no relevance to humans due to species-specific metabolism * No demonstrated potential for dermal irritation or sensitisation. |
| OECD |  | 2001 | * Different strains of rats may account for high variability in LD50 values. |
| US NIOSH |  | 1994 | * Revised IDLH based by toxicological analogies to both isobutyl alcohol and n-butyl alcohol. |

### 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 | — |
| NICNAS | — |
| EU Annex | — |
| ECHA | NA |
| ACGIH | Carcinogenicity – A4 |
| DFG | — |
| SCOEL | NA |
| HCOTN | NA |
| 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 |
| --- |
| |  |  |  |  | | --- | --- | --- | --- | | Adverse effects in human case study: | no |  |  | | Dermal LD50 ≤1000 mg/kg: | no |  |  | | 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 not warranted** | |

### IDLH

| Is there a suitable IDLH value available? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 74.1 |
| --- | --- |
| 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.

Deutsche Forschungsgemeinschaft (DFG) (2003) tert-Butyl alcohol – MAK value documentation.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) 2-Propanol, 2-methyl-: Human health tier II assessment – IMAP report.

Organisation for Economic Cooperation and Development (OECD) (2001) SIDS initial assessment profile – n-butyl alcohol.

Tenth Adaptation to Technical Progress Commission Regulation (EU Annex) 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 National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – tert-Butyl alcohol.