# Methyl tert-butyl ether

| CAS number: | 1634-04-4 |
| --- | --- |
| Synonyms: | Tert-butyl methyl ether, 2-methoxy-2-methylpropane, 2-methyl-2-methoxypropane,  methyl-1,1-dimethyl ether, MTBE |
| Chemical formula: | C5H12O |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **50 ppm (180 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 50 ppm (180 mg/m3) is recommended to protect for irritation, central nervous system (CNS) effects and possible developmental effects in exposed workers.

The previous STEL of 75 ppm (275 mg/m3) is recommended to be withdrawn as there is a lack of evidence for immediate acute toxicity within ten times of the recommended TWA.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

Methyl tert-butyl ether is used almost exclusively as an octane enhancer in fuel and as a petrol additive in unleaded fuel to reduce unburnt hydrocarbon emission.

The critical effects of exposure are irritation and CNS effects. A NOAEC for short-term exposure at 50 ppm is identified in a chamber study in male volunteers (ACGIH, 2018; SCOEL, 2006; DFG, 2000). This is the key study for the derivation of a TWA and is supported by data from other human and animal studies. A LOEC of 75 ppm is reported for CNS effects, feelings of heaviness in the head and mild mucosal irritation, in volunteers exposed for three hours (SCOEL, 2006). A two-generation study in rats reported a NOEC of 400 ppm for dams and offspring. A NOAEC for repeated inhalation exposure in rats at 800 ppm is based on effects on neurobehavioral function (ACGIH, 2018). A NOEC of 400 ppm is reported in mice for liver toxicity (DFG, 2000).

A TWA of 50 ppm is consistent across primary sources and is expected to be protective of effects on the CNS. The recommended TWA of 50 ppm is considered sufficiently low to protect for effects from short-term exposures marginally above this concentration and therefore a STEL is not recommended.

## 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 available data in animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 25 ppm (92 mg/m3); STEL: 75 ppm (275 mg/m3) | |
|  |
| ACGIH 2002 TLV-TWA: 50 ppm (180 mg/m3) |
| TLV-TWA recommended to protect for nasal effects and sensory irritation effects.  Summary of data:   * TLV-TWA stated as based on the following: * no symptoms noted in a chamber study of 10 subjects exposed at 50 ppm * NOAEC for repeated inhalation exposure of rats at 800 ppm * NOAEC of 400 ppm in rats from a two-generation study * renal toxicity noted in rats (both the dams and offspring) following inhalation at 300 and 3,400 ppm, * rounding according to ACGIH methodology.   Human data:   * Medicinal use in gallstone treatment: * complaints of headache, nausea, nasal congestion and eye irritation in personnel and other visitors * no air concentrations reported * Chamber study involving 10 male volunteers exposed at 5, 25 and 50 ppm for 2 h with light exercise: * solvent smell increased with increasing concentrations; initial solvent smell declined slowly * increase in nasal blocking/congestion or swelling over time but without a dose–response relationship * no other effects reported at all concentrations * Chamber study with 37 volunteers exposed for 1 h at 1.39 ppm: * based on questionnaire no headaches or nasal irritation * no effects on neurobehavioural outcomes * other chamber studies have supported these conclusions (no further information) * Increased self-reporting of acute symptoms which consisted of headache, dizziness, nausea, dyspnoea or irritation of saliva excretion in tanker drivers exposed at 3–98 mg/m3 (≈1–27 ppm) compared to controls.   Animal data:   * LD50: >10 mL/kg (rabbits, dermal) * Respiratory irritation study in mice: * slight sensory irritation at 300 mg/m3 (≈84 ppm) * severe irritation at 30,000 mg/m3 (8,333 ppm) * Rats exposed *via* inhalation at 0, 800, 4,000 or 8,000 ppm for 13 wk; sub-chronic neurotoxicity was measured; study authors reported a NOAEC of 800 ppm in rats for persistent or cumulative effects on neurobehavioral function * 24 mo inhalation study in rats exposed at 0, 400, 3,000, or 8,000 ppm: * NOAEC of 400 ppm for chronic nephropathy * NOAEC of 8,000 ppm for oncogenic effects * Male rats exposed for 6 h/d, 5 d/wk for 12 wk at 300, 1,300 or 3,400 ppm were mated to female rats exposed for 3 wk at the same concentrations; exposures continued through the mating period, during subsequent gestation and from days 5 to 21 of lactation * renal toxicity as dilated renal pelvis was noted in dams at 300 and 3,400 ppm and in offspring * 2-generation study in rats; exposed via inhalation at 0, 400, 3000 or 8000 ppm for 6 h/d for 10 wk: * NOEC of 400 ppm for adults and offspring * no increased risk to the offspring in the absence of adult toxicity * effects identified at higher doses hypoactivity ataxia, reduced bw gain and food consumption, increased liver weight.   No skin notation warranted based on available data.  Insufficient data to recommend a sensitiser notation or a TLV-STEL. |
| DFG 2000 MAK: 50 ppm (180 mg/m3) |
| MAK recommended to protect for irritation and the impairment of CNS functions.  Summary of additional data:   * Evidence of tumours in rats following long-term inhalation and oral exposure; not likely relevant to humans; concentrations and doses that do not cause non-neoplastic effects in the target organs are also not associated with an increased cancer risk * NOEC of 400 ppm in mice; liver toxicity; long-term study (no further information) * MAK based on studies with volunteers reporting a threshold value of >50 ppm for acute irritation and neuropathy effects (cited by ACGIH, 2018). |
| SCOEL 2006 TWA: 50 ppm (183.5 mg/m3); STEL: 100 ppm (367 mg/m3) |
| TWA and STEL recommended to protect for irritation and CNS effects in workers.  Summary of additional data:   * TWA and STEL based on: * LOEC of 75 ppm in volunteers; 3 h exposure; effects on simple reaction time, sway posturography, feeling of heaviness in the head and mild mucosal irritation * NOEC for short-term exposure of 50 ppm (cited by ACGIH, 2018) * Available data suggest that the dermal route is of minor importance. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2014 | * LD50:>2,000 mg/kg (rats, dermal) * Negative results for skin sensitisation in animals * 1-gen reproductive toxicity study in rats; NOAEC of 250 ppm for F1 animals; no further information * Critical effect considered to be skin irritation. |

### 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 | — |
| EU Annex | NA |
| ECHA | — |
| ACGIH | Carcinogenicity – A3 |
| DFG | Carcinogenicity – 3B |
| SCOEL | — |
| 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: | 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? | No |
| --- | --- |

## Additional information

| Molecular weight: | 88.15 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 3.60 mg/m3; 1 mg/m3 = 0.28 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) (2002) tert-Butyl methyl ether – MAK value documentation.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2006) Recommendation from the Scientific Committee on Occupational Exposure Limits for tert-butyl methyl ether. SCOEL/SUM/110.

International Agency for Research on Cancer (IARC) Some chemicals that cause tumours of the kidney or urinary bladder in rodents and some other substances. IARC Monographs – 73.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Propane, 2-methoxy-2-methyl: Human health tier II assessment – IMAP report.