# Mesityl oxide

| CAS number: | 141-79-7 |
| --- | --- |
| Synonyms: | Isobutenyl methyl ketone, isopropylidene acetone,  4-methyl-3-pentene-2-one |
| Chemical formula: | C6H10O |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **2 ppm (8.1 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **1,400 ppm (LEL)** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 2 ppm (8.1 mg/m3) is recommended to protect for local irritation in exposed workers.

## Discussion and conclusions

Mesityl oxide is used as a solvent, flotation agent in ore purification and insect repellent.

Critical effects of exposure are irritation of the eyes, skin and upper respiratory tract and potential narcosis at higher concentrations as observed in animals (ACGIH, 2018; DFG, 2016).

Limited human exposure data indicate eye and nasal irritation occur in less than 15 minutes at concentrations of 25 and 50 ppm, respectively (ACGIH, 2018). A LOAEC of 31 ppm (lowest tested concentration) for nasal irritation is reported in a sub‑chronic inhalation study with rats (DFG, 2016).

In the absence of sub-chronic and chronic human exposure data, the DFG (2016) MAK is based on the extrapolated NOAEC of 5 ppm for nasal inflammation in rats and halved to account for differences in experimental conditions and workplace exposures, which results in the recommended value of 2 ppm (DFG, 2016). A TWA of 2 ppm is recommended to be adopted from DFG (2016) and is expected to be protective of irritation effects in exposed workers. The recommended TWA is also considered to protect for potential narcosis in workers exposed at higher concentrations.

A STEL is not warranted as the recommended TWA is expected to be sufficiently protective of irritation that occurs at 25 ppm in humans and narcosis observed in animals above 250 ppm.

## 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 evidence.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 15 ppm (60 mg/m3); STEL: 25 ppm (100 mg/m3) |
|  |
| ACGIH 2001 TLV-TWA: 15 ppm (60 mg/m3); TLV-STEL: 25 ppm (100 mg/m3) |
| TLV-TWA and TLV-STEL intended to protect for irritation to the eyes and mucous membranes and narcosis at higher concentrations; adverse liver and kidney effects are also reported at higher concentrations in animals.  Summary of data:  TLV-STEL based on reports of eye irritation beginning at 25 ppm in exposed volunteers and workers. TLV-TWA recommendation appears to be based on weight of evidence that indicates a threshold of 15 ppm is protective of local irritation and narcosis and liver/kidney damage at higher concentrations, but its derivation is not discussed.  Human data:   * Eye irritation at 25 ppm and nasal irritation at 50 ppm in volunteer study (3–5 min):   + unpleasant taste persisted for 3–6 h   + cited study concludes 25 ppm is the highest satisfactory exposure for an 8 h shift, i.e. NOAEC * Dyspnoea, headache and vertigo predicted to occur at 100 ppm (no further information provided) * Additional citation states 25 ppm as the threshold for comfort in exposed workers although eye irritation is noted at this concentration * Eye irritation reported at 25 ppm for mesityl oxide may be more severe than that caused by structurally related saturated ketones.   Animal data:   * Eye and upper respiratory tract irritation at 13,000 ppm (rabbits, 30 or 90 min); lethal at 24,000 ppm (mice, 23 min), symptoms included dyspnoea, convulsions and narcosis:   + no gross changes to organ tissue found in necropsy * Oral LD50: 1,000 mg/kg (rabbits), 1,120 mg/kg (rats) * Pulmonary haemorrhage, renal tubular degeneration, distention of GIT and liver necrosis at 13,000 ppm in repeat inhalation study (mice, 30 min/d, 6 d); no fatalities at 700 ppm * NOAEL: 50 ppm in sub-chronic inhalation study (rats, guinea pigs, 8 h/d, 5 d/wk, 6 wk); eye and upper respiratory irritation reported at 250 and 500 ppm, narcotic effects at 500 ppm * No mutagenicity, carcinogenicity or ADME data presented.   Insufficient data to recommend notations for carcinogenicity, skin absorption or sensitisation. |
| DFG 2015 MAK: 2 ppm (8.1 mg/m3) |
| Summary of additional data:  Local eye, skin and respiratory tract irritation considered critical effects.  Current MAK based on a LOAEC of 31 ppm for nasal secretions and inflammatory response in sub-chronic inhalation study in rats. The incidence of these effects is considered low enough to extrapolate a NAEC based on relationship for signs of upper respiratory tract irritation between rodents and humans. A NAEC is extrapolated using the available LOAEC from sub-chronic study in absence of a NOAEC from chronic toxicity studies (DFG, 2018). Division of the LOAEC by 6 results in a NAEC of 5 ppm in humans and accounts for chronic exposure. The NAEC is further halved to account for differences in experimental conditions and the workplace and rounded down to arrive at the MAK of 2 ppm.  The previous 2007 MAK of 5 ppm also relied on the LAOEC of this study but was set at 5 ppm and did not account for differences in experimental conditions and the workplace exposure.  Skin notation recommended based on analogy to structurally related saturated ketones, such as methyl ethyl ketone, which demonstrate skin penetration and resultant systemic toxicity.  Negative results in maximisation test with guinea pigs do not warrant a sensitiser notation.  Animal data:   * RD50: 61 ppm (mice, 15 min) * LD50: 5,150 mg/kg (rabbits, dermal) * LOAEC: 31 ppm for nasal secretion and nasal epithelial exudate in sub-chronic inhalation study (rats, n=24/group, 6 h/d, 7 d/wk, 49 d); adverse effects only reported in 10/24 animals at 31 ppm, exudate from respiratory epithelium at 103 ppm and inflammation of the respiratory tract at 302 ppm * Reduced body weight and activity at 125 ppm, lowest tested dose, in repeat inhalation reproductive study (rats, GD 0–19); no substance-related pathological findings * 0.5 mL of undiluted substance causes irritation to skin (rabbits, semi-occlusive, 4 h); reversible within 15 d * Negative results in standardised maximisation test; induction with 10% in paraffin or undiluted substance, challenge with undiluted substance after 24 and 48 h (guinea pigs) * Narcosis and death following dermal application of 0.1 mL of substance (mice, 8 h); unclear if observed systemic effects due to dermal absorption or inhalation from evaporated substance * Negative mutagenicity *in vitro* in bacteria and *in vivo* in a micronucleus assay with mice.   Insufficient data to assign a carcinogenicity notation. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2004 TWA: 15 ppm (60 mg/m3) |
| Summary of additional data:  Insufficient data to derive HBROEL. Based on adverse haematological effects reported in rabbits at 25 ppm in a repeat inhalation study. The agency considers the current administrative OEL of 15 ppm at least an order of magnitude too high.  Animal data:   * Anaemia and decreased white blood cell count at 25 ppm (rabbits, 4 h/d, 5 d). |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| ECHA |  | 2019 | * Non-mutagenic *in vitro* in bacteria and *in vivo* in mice * DNEL adopted from previous 2007 DFG MAK of 5 ppm, which is supported by a derivation based on the LOAEL of 25 ppm for irritation in volunteers exposed for <15 min (also cited in ACGIH, 2018); assessment factor of 5 applied to account for intraindividual variation to equally arrive at the inhalation DNEL of 5 ppm. |
| OECD |  | 1997 | * Negative mutagenicity results *in vitro* in bacteria and *in vivo* in mice. |
| US NIOSH |  | 1994 | * IDLH based on being 10% of the lower explosive limit of 1.4%. |

### 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 | NA |
| EU Annex | — |
| ECHA | — |
| ACGIH | — |
| DFG | H (skin) |
| 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 |
| --- |
| |  |  |  |  | | --- | --- | --- | --- | | 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? | Yes, based on LEL |
| --- | --- |

## Additional information

| Molecular weight: | 98.14 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 4.01 mg/m3; 1 mg/m3 = 0.250 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) (2018) List of BAT and MAK Values 2018 – Report 54.

Deutsche Forschungsgemeinschaft (DFG) (2016) 4-Methyl-3-penten-2-on – MAK value documentation, German language edition.

Deutsche Forschungsgemeinschaft (DFG) (2007) 4-Methyl-3-penten-2-on – MAK value documentation, German language edition.

European Chemicals Agency (ECHA) (2019) Mesityl oxide – REACH assessment.

Health Council of the Netherlands (HCOTN) (2004) 4-Methylpent-3-en-2-one. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/104.

Organisation for Economic Cooperation and Development (OECD) (1997) SIDS initial assessment profile – Mesityl Oxide.

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 – Mesityl oxide.