# 5-Methylheptan-3-one

| CAS number: | 541-85-5 |
| --- | --- |
| Synonyms: | Amyl ethyl ketone, EAK, ethyl sec-amyl ketone,  ethyl 2-methylbutyl ketone, 2-methylbutyl ethyl ketone, 3-methyl-5-heptanone, 5-methyl-3-heptanone |
| Chemical formula: | C8H16O |
| Structural formula: | — |

Workplace exposure standard (retained)

| TWA: | **10 ppm (53 mg/m3)** |
| --- | --- |
| STEL: | **20 ppm (107 mg/m3)** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **100 ppm** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 10 ppm (53 mg/m3)is recommended to protect for neurotoxic effects and local irritation in exposed workers.

A STEL of 20 ppm (107 mg/m3) is recommended to protect for acute irritation of the eyes, nose and throat in exposed workers.

## Discussion and conclusions

5-Methylheptan-3-one is used as a solvent for nitrocellulose-alkyd, nitrocellulose-maleic and vinyl resins.

Critical effects of exposure include irritation of the eyes, nose and throat and neurotoxicity.

No irritation reported in volunteers exposed for five minutes at 5 ppm (NOAEC). In this study, mild nasal irritation was reported at 25 ppm (LOAEC) with increased irritation at 50 ppm and additional headache and nausea at the highest concentration of 100 ppm (DFG, 2001; SCOEL, 1991). A NOAEL of 82 mg/kg/day based on neuropathy is reported in a 13-week rat gavage study (ACGIH, 2018; DFG, 2001). Based on this NOAEL, ACGIH (2018) extrapolated the human equivalent airborne concentration exposure at NOAEC of 110 ppm and used this NOAEC to derive a TLV-TWA of 10 ppm (53 mg/m3). DFG (2001) and SCOEL (1991) also derived an OEL of 10 ppm (53 mg/m3).

The SWA TWA of 10 ppm (53 mg/m3) and the STEL of 20 ppm (107 mg/m3) (SCOEL, 1991) are recommended be retained to limit irritant and neurotoxic effects. A STEL is recommended to protect for irritation from acute exposures of 50 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.

There are insufficient data to recommend a skin notation.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 10 ppm (53 mg/m3); STEL: 20 ppm (107 mg/m3) | |
|  |
| ACGIH 2007 TLV-TWA: 10 ppm (52.4 mg/m3) |
| TLV-TWA recommended to minimise potential neurotoxic effects.  TLV-TWA based on the conversion of a NOAEL in rats of 82 mg/kg/d to airborne concentration equivalent of 574 mg/m3 (110 ppm) *via* generic factors; no further specifics provided  Summary of data:  No human studies available.  Animal data:   * RD50: 760 ppm (3,980 mg/m3) in mice * Male rats dosed *via* gavage at 0, 82, 410 or 820 mg/kg 5 d/wk for 13 wk; rats subject to functional observational battery of tests along with body weight, feed consumption, haematology, cell morphology, clinical chemistry and neuropathology: * the functional observational battery included procedures to detect unusual body positions or activity level, compromised coordination of movement or gait, any unusual or bizarre behaviour, and other indications of neurotoxicity, including but not limited to limb grip strength, convulsions, tremors, and lacrimation * an observation from the battery of reduced vocalisation established the LOAEL of 82 mg/kg/d * no NOEL for reduced vocalisation was identified: effect was not considered adverse * NOAEL of 82 mg/kg/d based on 2 observations of reduced lifting of the tail and overall reduced activity * NOAEL of 410 mg/kg/d for 9 observations: unkempt hair coats [p <0.0001], exophthalmos [p ≈0.03], minor tremors [p ≈0.05], failure to respond to touch [p ≈0.006], hypotonic gait [p <0.002], tail-dragging [p=0.0001], lateral deviation of the limbs [p ≈0.006], difficulty hopping [p ≈0.008], and soft muscle tone [p ≈0.01] * no difference in body weight or feed consumption from control rats at 82 mg/kg/d * body weights were 9% less than control rats on average and consumed slightly less feed at 410 mg/kg/d, but these differences were not statistically significant * average body weights were 24% lower than control rats (statistically significant at p < 0.05) and consumed 12% less feed on average at 820 mg/kg/d * no significant differences between exposed and unexposed rats in haematology and cell morphology * plasma concentrations of alanine aminotransferase (ALT) reduced; the 82-mg/kg/d group had 14% less ALT than control rats; the 410-mg/kg/d group had 30% less and the 820-mg/kg/d group had 32% less; this effect not necessarily considered adverse * pathological examination revealed damage to the tibial and sciatic nerves, including infolding of the myelin sheath into the axon, Wallerian degeneration, axonal swelling and thinning of the myelin sheath over swollen axons; for both nerves, the NOAEL for infolding of the myelin sheath into the axon, Wallerian degeneration, and axonal swelling was 82 mg/kg/d; the NOAEL for thinning of the myelin sheath over swollen axons was 410 mg/kg for both nerves * authors concluded 82 mg/kg/d as the NOAEL for the entire study * Airborne concentration equivalent of NOAEL is 574 mg/m3 (110 ppm); 70 kg human inhaling 10 m3 in an 8-h workday.   TWA justified by the equivalent airborne concentration; no further derivation.  Insufficient data to recommend a skin, sensitiser or carcinogenicity notation or a TLV-STEL. |
| DFG 2001 MAK: 10 ppm (53 mg/m3) |
| MAK recommended to protect for local irritation and neurotoxicity effects.  Summary of additional data:   * Reported odour threshold of 5 and 6 ppm * A 5-min exposure study on volunteers reported the following: * 5 ppm tolerated with no symptoms of irritation * 25 ppm slight irritation of mucous membranes * 50 ppm irritation of eyes, nose and throat * 100 ppm strong irritation and headache and nausea * Groups of 5 male rats (no other details) were given 100, 500 or 1000 mg/kg/d by gavage for 13 wk: * at 1,000 mg/kg/d peripheral neuropathy occurred; seen from clinical observations and functional tests carried out: stumbling and paralysis of the rear extremities, decreased reflexes and upright reflexes, reduced tone of the hind leg muscles, reduced grip strength of the hind legs as well as diarrhoea, reduced activity, unkempt fur, salivation and reduced body weight * similar effects to a lesser extent as those reported at 1000 mg/kg/d at 500 mg/kg/d * no clinical effect reported at 100 mg/kg/d * clinical chemistry and haematology were normal * Dose of 100 mg/kg/d reported as having a corresponding airborne equivalent concentration of ~100 ppm; no derivation provided; basis for MAK. |
| SCOEL 1991 TWA: 10 ppm (53 mg/m3); STEL: 20 ppm (107 mg/m3) |
| OELs recommended to protect for nasal irritation.  Summary of additional data:   * Based on same 5 min exposure study as cited by DFG (2001) * No information on toxicity following repeat exposure; considers acute data acceptable provisionally. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

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

### IDLH

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

## Additional information

| Molecular weight: | 128.21 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 5.24 mg/m3; 1 mg/m3 = 0.191 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) (2001) 5-methylheptan-3-on – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (1991) Recommendation from the Scientific Committee on Occupational Exposure Limits for 5-methylheptan-3-one. SCOEL/SUM/9.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – 5-Methyl-3-heptanone.