# 1-Methyl-2-pyrrolidone

| CAS number: | 872-50-4 |
| --- | --- |
| Synonyms: | 1-Methylpyrrolidin-2-one |
| Chemical formula: | C5H9NO |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **20 ppm (80 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

A TWA of 20 ppm (80 mg/m3) is recommended to protect for irritation of the upper respiratory tract, developmental effects and central nervous system (CNS) effects in exposed workers.

The previous STEL is recommended to be withdrawn as there is a lack of evidence for immediate acute toxicity within ten times the recommended TWA.

## Discussion and conclusions

The primary use of 1-methyl-2-pyrrolidone is as a solvent. It is used in a wide range of applications in the paints and petrochemical industries, the microelectronics industry and as a substitute for chlorinated solvents.

The critical effects of exposure are upper respiratory tract irritation and developmental and CNS effects.

No effects, other than odour detection and slight perception of annoyance, were observed in male volunteers exposed at 20 ppm including peaks of up to 40 ppm (DFG, 2019; SCOEL, 2007). Irritation was not observed in volunteers exposed at 12.2 ppm for eight hours a day for four days (DFG, 2019). A NOAEC of 61 ppm for pregnant workers was reported by NICNAS (2013) based on reduced foetal body weight in rats. A NOAEC of 50 ppm for developmental effects was established in multi-generational study in rats based on delayed weight development in F1 (reversible after weaning) and a CNS effect, diminished reaction behaviour in F0 animals at higher concentrations (DFG, 2019). Based on this study, DFG (2019) derived a MAK of 20 ppm. SCOEL (2007) derived an OEL of 10 ppm based on a different reproductive toxicity study in animals. OARS (2010) also derived a TWA of 10 ppm.

A TWA of 20 ppm (80 mg/m3) by DFG is recommended based on the fact that adverse effects were absent at concentrations up to 40 ppm in humans and the NOAEC of 50 ppm is identified for minor reproductive effects in animals. The recommended TWA is considered to protect for irritation of the upper respiratory tract and developmental effects and possible CNS effects.

The evidence does not support the recommendation of a STEL and the recommended TWA is adequately protective of acute exposures.

## 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 recommended based on systemic effects associated with dermal exposure in humans.

# Appendix

### Primary sources with reports

| **Source Year set Standard** |
| --- |
| SWA 1991 TWA: 25 ppm (103 mg/m3); STEL: 75 ppm (309 mg/m3) | |
|  |
| ACGIH NA NA |
| No report. |
| DFG 2019 MAK: 20 ppm (82 mg/m3) |
| MAK recommended to protect for irritation of the upper respiratory tract, fetotoxicity and neurotoxicity.  Summary of data:   * MAK of 19 ppm set in 1994 based on NOAEC of 50 ppm from multi-generational study in rats (cited below); no specific derivation provided * In 2006 supplement, in accordance with the preferred value approach, MAK adjusted to 20 ppm; justified with human evidence.   Human data:   * Male volunteers exposed at 20 ppm for 8 h, with and without peaks of 40 ppm, did not show adverse irritant or cognitive effects; justification for MAK, adjustment in 2006 * Irritation not observed in volunteers exposed at 12.2 ppm 8 h/d for 4 d * Estimated the amount absorbed only through the skin during exposure at the level of the MAK value would be 27% of the amount absorbed via inhalation; 21% of the total uptake * A pregnant worker exposed during first 20 wk of pregnancy including a spill on skin and clothing; delayed embryonic development was diagnosed in gestation wk 25 and the child was stillborn in wk 31; other risk factors ruled out.   Animal data:   * LC50: ≈771–2,135 ppm (rats) * NOAEC of 50 ppm multi-generational study in rats; 7 d/wk, 6 h/d for 100 d; delayed weight development in F1 (reversible after weaning); F0 animals, a CNS effect, diminished reaction behaviour. |
| SCOEL 2007 TWA: 10 ppm (40 mg/m3); STEL: 20 ppm (80 mg/m3) |
| TWA and STEL recommended to protect for irritation, narcosis and systemic effects including reproductive toxicity.  Summary of additional data:   * OELs based on the evidence of respiratory irritation and chemosensory effects, both in humans and animals and reproductive toxicity in studies in experimental animals; no specific derivation provided.   Human data:   * Severe eye irritation and headache in workers exposed at up to 70 ppm (no additionalinformation) * 16 healthy young male volunteers exposed at 2.5 ppm (10 mg/m3), 10 ppm (40 mg/m3) 20 ppm (80 mg/m3) and 40 ppm (160 mg/m3), absence of effects other than odour detection and slight perception of annoyance following exposure up to 40 ppm (based on same study cited by DFG, 2017); 10 ppm provided adequate margin of safety in support and basis for TWA; no further information.   Animal data:   * NOAEL range of ≈50–125 ppm in rats, rabbits and mice for minor reproductive effects; decreased pup weight and pup weight gain in the presence of maternal toxicity; application of UF of 5 results in 10 ppm; used to recommend TWA * 2 yr inhalation study in rats; minimal inflammation of the lung and slight systemic toxicity in male rats at 18 mo, but not at 24 mo at 100 ppm; considered borderline LOAEL/NOAEL. |
| OARS/AIHA 2010 TWA: 10 ppm (40 mg/m3) |
| No additional data. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| **Source** |  | **Year** | **Additional information** |
| --- | --- | --- | --- |
| NICNAS |  | 2013, 2018 | * Dermal NOAEL of 237 mg/kg/d; reduced numbers of pups, reduced foetal body weight and indications of retarded skeletal development at the next higher dose of 750 mg/kg/d * NOAEC of 0.247 mg/L; 6 h/d inhalation in rats; based on statistically significant decreases in foetal body weight at the next higher dose (0.494 mg/L) * Derived no effect level (DNEL) for pregnant workers were 247 mg/m3 or 61 ppm (NOAEC); reduced foetal body weight in rats. |

### 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 | Skin |
| HCIS | — |
| NICNAS | — |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | NA |
| DFG | H (skin) |
| SCOEL | Skin |
| 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: | 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: | 99.13 |
| --- | --- |
| 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) (2019) N-Methyl-2-pyrrolidone (vapour) – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2007) Recommendation from the Scientific Committee on Occupational Exposure Limits for N-Methyl-2-Pyrrolidone. SCOEL/SUM/119.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) 2-Pyrrolidinone, 1-methyl: Human health tier II assessment – IMAP report.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) 2-Pyrrolidinone, 1-methyl: Human health tier III assessment – IMAP report.

Occupational Alliance for Risk Science (OARS) (2010) Workplace environmental exposure level – Methyl-2-Pyrrolidone, n-.