# N-Methyl aniline

| CAS number: | 100-61-8 |
| --- | --- |
| Synonyms: | N-methylaminobenzene, monomethyl aniline |
| Chemical formula: | C7H9N |
| Structural formula: | — |

Workplace exposure standard (interim)

| TWA: | **0.5 ppm (2.2 mg/m3)** |
| --- | --- |
| STEL: | — |
| Peak limitation: | — |
| Notations: | **Sk.** |
| 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 0.5 ppm (2.2 mg/m3) is recommended to protect for methaemoglobin formation and related effects in exposed workers.

Given the limited data available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

## Discussion and conclusions

N-methylaniline is used as an acid acceptor, a solvent, and in organic syntheses.

The critical effect of exposure is methaemoglobin formation. Very limited data exists in humans and animals. The toxicology profile is likely to be closely related to that of aniline (ACGIH, 2018; SCOEL, 2012).

ACGIH, (2018) report a safety limit of 2 ppm based on a study in animals. A LOAEC of 2.9 ppm is reported in rats for reduced haemoglobin values, increased reticulocyte counts and the increased accumulation of brown pigment in the spleen (DFG, 2017). Animal data indicate that N‑methylaniline is at least twice more potent at inducing methaemoglobin than aniline (DFG, 1987; SCOEL, 2014). Both DFG (2017) and SCOEL (2014) base OELs on aniline but derive different values. Animal studies clearly indicate that N-methylaniline is well absorbed through intact skin (ACGIH, 2018, DFG, 2017; SCOEL, 2014).

Given the limited data and uncertainties that surround analogy with aniline, the SWA TWA of 0.5 ppm (2.2 mg/m3) is recommended to be retained. This TWA is cited to be protective of methaemoglobin formation in exposed workers. Insufficient data exists regarding short-term exposures to support the recommendation of a STEL as recommended by SCOEL.

Noting the uncertainties in the data it is recommended that an investigation of additional data sources is undertaken at the next scheduled review.

## 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 evidence of dermal absorption in animals and the potential to contribute to the systemic effects.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 0.5 ppm (2.2 mg/m3) | |
| Absorption through the skin may be a significant source of exposure. |
| ACGIH 2001 TLV-TWA: 0.5 ppm (2.2 mg/m3) |
| TLV-TWA recommended to minimise the potential for the induction of anoxia and cyanosis due to the formation of methemoglobinemia.  Summary of data:   * Clinical toxicology resembles aniline.   Human data:   * No toxicological data in humans available * No reports of human intoxication from exposure to N-methylaniline; based on similarity to aniline, overexposure expected to induce methemoglobinemia with signs of cyanosis in the lips, nose, and earlobes, weakness, dizziness and severe headache.   Animal data:   * 3,000 mg/kg on intact rabbit skin resulted in death in 1 h or more; no further information * One study reported the following: * deaths in rabbits, guinea pigs and rats exposed ≤130 times, 7 h inhalation exposures at 7.6 ppm; * deaths in cats exposed at 27 ppm exposures ≤58 times * one dog survived 50 exposures at 86 ppm * one monkey survived 130, 7 h exposures at 2.3 ppm * safety limits reported as 2.4–7.6 ppm * methemoglobinemia (at 7.6 ppm) and the formation of Heinz bodies (at 2.4 ppm) in rats * pulmonary effects ranging from oedema to interstitial pneumonia, as well as occasional centrilobular hepatic necrosis and moderate kidney damage.   TLV-TWA is justified on the view that 2 ppm offers a small margin of safety; based on the functional anaemia found in animals exposed at 2.4 ppm.  Skin notation warranted as it is readily absorbed through the skin in amounts that can contribute substantially to systemic poisoning; no further information. |
| DFG 2017 MAK: 0.5 ppm (2.2 mg/m3) |
| MAK based on the critical effect of methaemoglobin formation.  Summary of addition data:   * No suitable human data to derive MAK * LOAEC of 13 mg/m3 (2.9 ppm); 28 d inhalation study in rats; reduced Hb values, increased reticulocyte counts and the increased accumulation of brown pigment in the spleen * TLV-TWA basis: considered 2.7 times more potent than aniline in forming methaemoglobin; aniline TLV-TWA 2 ppm; TLV-TWA of 0.5 ppm considered suitable * Absorption through intact skin may substantially contribute to toxicity: * diluted aqueous solution; 2,000 cm2 skin/1 h results in 68–951 mg absorption. |
| SCOEL 2012 TWA: 0.2 ppm (0.89 mg/m3); STEL: 0.5 ppm (2.2 mg/m3) |
| TWA and STEL recommended to protect for methaemoglobin formation and toxic effects on the haematopoietic system with erythrocytotoxicity and effects on the spleen.  Summary of additional data:   * OELs based on analogy to aniline * Animal data indicate that N-methylaniline is twice more potent at inducing methaemoglobin than aniline * Aniline TWA OEL 0.5 ppm and STEL 1 ppm * Animal studies clearly indicate that NMA is well absorbed through the intact skin. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | ND | * No information. |

### 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 | NA |
| EU Annex | NA |
| ECHA | — |
| ACGIH | Skin |
| DFG | Carcinogenicity – 3B, 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 |
| --- |
| |  |  |  |  | | --- | --- | --- | --- | | Methyl aniline  Adverse effects in human case study: |  |  |  | | 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%: | yes | 2.00 |  | |  |  | **insufficient data to assign a skin notation** | | |

### IDLH

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

## Additional information

| Molecular weight: | 107.15 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 4.38 mg/m3; 1 mg/m3 = 0.229 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) (2017) N-Methylaniline – 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) (2012) Recommendation from the Scientific Committee on Occupational Exposure Limits for N-Methylaniline. SCOEL/SUM/178.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Monomethyl aniline.