# N,N-Dimethylaniline

| CAS number: | 121-69-7 |
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| Synonyms: | Dimethylaniline, Dimethylaminobenzene,  N,N-Dimethylbenzenamine, N,N-Dimethylphenylamine |
| Chemical formula: | C8H11N |
| Structural formula: | — |

Workplace exposure standard (retained)

| TWA: | **5 ppm (25 mg/m3)** |
| --- | --- |
| STEL: | **10 ppm (50 mg/m3)** |
| Peak limitation: | **—** |
| Notations: | **Carc. 2, 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 5 ppm (25 mg/m3) is recommended to protect for neurotoxic effects and anoxia due to the formation of methaemoglobin in exposed workers.

A STEL of 10 ppm (50 mg/m3) is recommended to protect for rapid formation of methaemoglobin in acutely exposed workers.

## Discussion and conclusions

N,N-Dimethylaniline is widely used in manufacturing as a solvent, an intermediate and reagent for dyes, a rubber vulcanising agent and as a catalyst (ACGIH, 2018; HCOTN, 2002).

The critical effects of exposure are methaemoglobinaemia and neurotoxicity. Limited human exposure data are available. The ACGIH derived a TLV-TWA of 5 ppm based on lower expected toxicity in comparison to aniline. N,N-dimethylaniline can be absorbed through the skin resulting in systemic toxicity effects including methaemoglobinaemia and central nervous system (CNS) depression (ACGIH, 2018). Death is reported following acute exposure at 50 ppm for four hours in rats (ACGIH, 2018).

The current TWA of 5 ppm is recommended to be retained. It is consistent across primary sources and, on the weight of evidence presented, is expected to be protective of effects on the CNS. A severe adverse effect (death) is evident at ten times the TWA (50 ppm) in animal studies (ACGIH, 2018) and the immediately dangerous to life and health value is reported at 100 ppm in analogy to aniline (NIOSH, 1994). Therefore, a STEL of 10 ppm is recommended in line with ACGIH (2018) to protect for listed effects in acutely exposed workers.

## Recommendation for notations

Classified as a category 2 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 due to rapid and significant dermal absorption and contribution to systemic effects.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 5 ppm (25 mg/m3); STEL: 10 ppm (50 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 5 ppm (25 mg/m3); TLV-STEL: 10 ppm (50 mg/m3) |
| TLV-TWA and STEL recommended to protect against methaemoglobinaemia, anoxia and neurotoxicity.  Summary of data  TLV-TWA and TLV-STEL are based on the premise that dimethylaniline is less toxic than aniline (TLV-TWA of 2 ppm); no further information presented.  Human data:   * Readily absorbed through skin, results in methaemoglobinaemia and depressant effect on CNS * Few reports of industrial experience available * Lowest lethal dose reported as 50 mg/kg * Toxicity in two workers: * one worker exposed only for a few minutes was unconsciousness and reported visual disturbances, noise in ears and intense abdominal pain * other worker was less severely poisoned after many hours of exposure * Similar symptoms as aniline poisoning.   Animal data:   * Rats are more susceptible to adverse effects than mice * LD50: 1,300–1,500 mg/kg (rats, oral); effects include cyanosis, nasal discharge and decreased activity * single oral administration of 50 mg/kg led to methaemoglobin formation in dogs * LD50: 1,770 mg/kg (rabbits, dermal) * Lowest lethal concentration of 250 mg/m3 (50 ppm) (rats, 4 h) following inhalation * 100 d continuous inhalation exposure led to anaemia, methaemoglobinaemia, cytopaenia and impairment of adrenal gland and liver function (male rats) * Doses up to 1,500 mg/kg/d, 14 d (rats) or 15 d (mice) or up to 500 mg/kg, 5 d/wk, 13 wk: * effects including lethargy, excessive salivation and tremors with cyanosis indicative of erythrocyte destruction and reduced blood oxygenation, possibly due to methaemoglobinaemia formation * NOEL: 30 mg/kg/d (mice, oral), rats more susceptible and no NOEL determined * Species difference in increased incidence of sarcomas or osteosarcomas in spleen or thymus reported in male rats in high dose group * no evidence of carcinogenicity in female rats and male mice, but evidence in female mice indicated incidence of squamous cell papillomas of the forestomach * fibrosis, haemosiderosis and fatty metamorphosis reported in male rats * No reproductive or developmental effects reported.   Inconclusive findings in genotoxicity studies due to mixed results; negative in *S. typhimurium* assays as high as 1,000 mg/plate, positive in mouse lymphoma assay, negative for rat hepatocytes and positive in SCE induction and chromosomal aberrations in Chinese hamster ovary cells following metabolic activation.  A skin notation is recommended due to rapid and significant dermal absorption and contribution to systemic effects.  Insufficient data to assign carcinogenicity classification or recommend a SEN notation. |
| DFG 1990 MAK: 5 ppm (25 mg/m3) |
| Summary of additional data:  Human data:   * One reported study in exposed workers (number not specified); significant increase in methaemoglobinaemia level reaching 5.2% in some exposed individuals; no exposure details.   Animal data:   * No additional information on carcinogenicity and genotoxicity. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2002 NA |
| Summary of additional data:   * No human data available * Limited evidence of carcinogenicity in animals. * Inconclusive findings with respect to genotoxicity due to mixed results; negative in *S. typhimurium* assays, positive in SCE induction and chromosomal aberrations but no primary DNA damage. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| US EPA |  | 2002 | * No available inhalation RfC * No available carcinogenic assessments evaluated * Oral RfD of 2×10-3 mg/kg/d based on LOAEL: 31.25 mg/kg/d (22.32 mg/kg/d) for splenomegaly, increased splenic haemosiderosis and haematopoiesis (mouse sub-chronic gavage bioassay). |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Insufficient data |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Insufficient data |
| **Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.** | |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Carc. 2, Skin |
| HCIS | Carcinogenicity – category 2 |
| NICNAS | Carc. Cat 3, Skin |
| EU Annex | NA |
| ECHA | Carc. 2 |
| ACGIH | Carcinogenicity – A4, Skin |
| DFG | Carcinogenicity – 3B, H (skin), |
| SCOEL | NA |
| 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 |
| --- |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Conclusion:** |  |  |  |  |  |  | |  |  | 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? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 121.19 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 5.03 mg/m3; 1 mg/m3 = 0.19 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 |
| --- | --- |
| 1991 | TLV-TWA of 5 ppm (25 mg/m3) and STEL of 10 ppm (50 mg/m3) |

## 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.

European Chemicals Agency (ECHA) (2019) N,N-Dimethylaniline – REACH assessment.

Deutsche Forschungsgemeinschaft (DFG) (1992) N,N-Dimethylaniline – MAK value documentation.

Health Council of the Netherlands (HCOTN) (2002) N,N-dimethylaniline. Evaluation of the carcinogenicity and genotoxicity. The Hague: Health Council of the Netherlands; publication no. 2002/05OSH.

International Agency for Research on Cancer (IARC) (1993) N,N-Dimethylaniline. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Benzenamine, N,N-dimethyl-: Human health tier II assessment – IMAP report.

US National Institute for Occupational Safety and Health (NIOSH) (1994). Immediately dangerous to life or health concentrations (IDLH) – N,N-Dimethylaniline.

US Environmental Protection Agency (US EPA) (2002). Chemical Assessment Summary – N,N-Dimethylaniline; CASRN 121-69-7. Integrated Risk Information System (IRIS).