# 5-nitro-o-toluidine

| CAS number: | 99-55-8 |
| --- | --- |
| Synonyms: | 2-Methyl-5-nitrobenzenamine, 5-nitro-2-toluidine, azoic diazo compound 12,  1-amino-2-methyl-5-nitrobenzene,  2-amino-4-nitrotoluene, 2-methyl-5-nitroaniline |
| Chemical formula: | C7H8N2O2 |
| Structural formula: | — |

Workplace exposure standard (new)

| TWA: | **1 mg/m3 (inhalable particulate matter)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 2** |
| 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 1 mg/m3 is recommended to protect for liver damage in exposed workers.

## Discussion and conclusions

5-Nitro-o-toluidine is the main component in over 35 technical dyestuff bases. It is used in wood stains and polishes and colour in detergents and paper (ACGIH, 2018 and NICNAS, 2014).

The critical effect of exposure is liver damage.

Limited human data are available. Accidental exposure in workers resulted in liver damage. However, recovery occurred following cessation of exposure (ACGIH, 2018). Deaths caused by liver failure are reported in individuals following ingestion of the chemical as a sweetener (NICNAS, 2014). However, exposure concentrations are not available. Based on a chronic feeding study in rats, a LOAEL of 2.5 mg/kg/day is identified (based on slight decrease in body weight) which is equivalent to an inhalation exposure of 17.5 mg/m3 (ACGIH, 2018).

A TWA of 1 mg/m3 as assigned by ACGIH (2018) is recommended to limit adverse effects on the liver.

## 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.

There are insufficient data to recommend a skin notation. A further review of literature is recommended as dermal absorption is expected to be a significant route of exposure as an aromatic nitroamine and limited human exposures reported.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA NA NA | |
|  |
| ACGIH 2007 TLV-TWA: 1 mg/m3 (inhalable particulate matter) |
| TLV-TWA recommended to minimise the potential for liver effects in exposed workers.  Summary of data:  Human data:   * 15 workers who manually handled 5-nitro-o-toluidine: * 3 hospitalised with acute liver dysfunction * 7 had signs of liver damage * protective equipment worn, however exposure likely due to removing respirator during breaks when powder not visible * concentration not known; recovery occurred following cessation of exposure.   Animal data:   * Induced methaemoglobinaemia in cats (by IP injection) and not in rabbits (oral doses at 500 mg/kg/d) * Varied results in sub-chronic study in rats; doses of 4.5–72 mg/kg/d for 3 wk reported decreased weight and deaths at all levels, while another 4 wk study with doses of   4.5–36 mg/kg/d recorded no deaths   * LOAEL: 2.5 mg/kg (rats, oral, 78 wk); slight decreased body weight towards end of study * Increased incidence of hepatocellular carcinomas in male and female mice fed 240 or 460 mg/kg/d for 78 wk * Dose-dependent malignant liver tumours observed following feeding at 1,200 or 2,400 ppm (mice, 24 wk) * Mutagenic in several strains of *S. typhimurium* * Positive results with *S. typhimurium* strain TA 1535 only when exogenous metabolic system was absent * Not mutagenic (with or without a metabolic system) in *E. coli* WP2uvrA.   Insufficient data to assign Skin or SEN notation or recommend TLV-STEL. |
| DFG 1993 Not assigned |
| Summary of additional data:   * LD50: 574 mg/kg (rat, oral); 600 mg/kg (mouse, oral) * IP injection of 600–700 mg/kg in guinea pigs caused marked CNS effects and increased methaemoglobin levels, then death generally within 4–10 h; * Daily IP injection of 100 mg/kg caused pronounced hair loss, weight loss, anaemia and death after 13–15 d; examination revealed enlarged liver and kidneys * No reports relating to effects following dermal or percutaneous administration; expected to be absorbed through intact skin like other aromatic nitroamines. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2014 | * Expected to be readily absorbed by all routes of exposure * Methaemoglobinaemia reported following excessive absorption in humans- no further information * Ingestion of the chemical as a sweetener caused death in individuals from liver failure; doses not reported; toxic effects included high fever, nausea, vomiting, swollen liver, jaundice and tendency to bleed * Considered genotoxic based on weight of evidence but limited evidence of carcinogenicity. |
| IARC |  | 1990 | * No additional information. |

### 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 | NA |
| HCIS | Carcinogenicity – category 2 |
| NICNAS | Carc. Cat. 3 |
| EU Annex | Carcinogenicity – category 2 |
| ECHA | NA |
| ACGIH | Carcinogenicity – A3 |
| DFG | NA |
| 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

| Insufficient data to assign a skin notation. |
| --- |

### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

| Molecular weight: | 152.16 |
| --- | --- |
| 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) (1993) 5-Nitro-o-toluidine – MAK value documentation.

International Agency for Research on Cancer (IARC) (1990) Volume 48, Some Flame Retardants and Textile Chemicals, and Exposures in the Textile Manufacturing Industry. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Benzenamine, 2-methyl-5-nitro: Human health tier II assessment – IMAP report.

Tenth Adaptation to Technical Progress Commission Regulation (EU) 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).