

# NITROMETHANE

**CAS number:** 75-52-5

**Synonyms:** Nitrocarbol, mononitromethane

**Chemical formula:**  $\text{CH}_3\text{NO}_2$

**Structural formula:** —

## Workplace exposure standard (retained)

**TWA:** 20 ppm (50 mg/m<sup>3</sup>)

**STEL:** —

**Peak limitation:** —

**Notations:** —

**IDLH:** 750 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 20 ppm (50 mg/m<sup>3</sup>) is recommended to protect for red blood cell (RBC) effects, respiratory tract irritation and adverse effects in the nasal cavity in exposed workers.

## Discussion and conclusions

Nitromethane is used as a chemical stabiliser for halogenated hydrocarbon solvents and aerosol propellants. It is also used as a chemical intermediate, rocket propellant and an explosive when mixed with ammonium nitrate.

Critical effects of exposure are RBC effects, respiratory tract irritation and adverse effects in nasal cavity as observed in animals. Limited human toxicological data are available. Nitromethane is considered to act as a weak narcotic and respiratory irritant in humans (ACGIH, 2018). There is a case report indicating two workers developed severe peripheral neuropathy following brief exposure (one to two months) but concentration was not reported (ECHA, 2019). A NOAEC of 94 ppm (235 mg/m<sup>3</sup>) is identified for microcytic anaemia, hyperplasia of the bone marrow and respiratory hyaline droplets in a 13-week study in rats and mice (ACGIH, 2018; ECHA, 2019). Liver neoplasms, Harderian gland adenomas and carcinomas and nose lesions, including effects on nasal cavity and respiratory tract, are reported in mice at doses as low as 188 ppm in a two-year inhalation study in rats and mice. However, no effects were reported in rats at 94 ppm in this study (ACGIH, 2018).

Based on the NOAEC of 94 ppm, the SWA TWA of 20 ppm (50 mg/m<sup>3</sup>) derived by ACGIH is recommended to be retained. Based on the weight of evidence, the recommended TWA is considered protective for RBC effects, respiratory tract irritation and nasal cavity changes.

## 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.

DRAFT

## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>1991</b>	<b>TWA: 20 ppm (50 mg/m<sup>3</sup>)</b>
<b>ACGIH</b>	<b>2001</b>	<b>TLV-TWA: 20 ppm (50 mg/m<sup>3</sup>)</b>
<p>TLV-TWA recommended to minimise the risk of adverse thyroid effects, nasal cavity changes and respiratory tract irritation.</p> <p>Summary of data:</p> <p>No specific derivation provided; based on adverse thyroid effects in rabbits at 98 ppm and non-neoplastic effects (nose lesions) in mice from 188 ppm.</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>• Likely human lethal dose 0.5–5.0 g/kg; no further information</li> <li>• Weak narcotic and respiratory irritant: <ul style="list-style-type: none"> <li>○ may cause liver damage with prolonged exposure</li> <li>○ mildly irritating to skin and mucous membranes</li> </ul> </li> <li>• No human case reports of exposure or epidemiological evidence presented in scientific literature.</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>• LD<sub>50</sub>: 1,440 mg/kg (mouse, oral); 1,210 mg/kg (rat, oral)</li> <li>• LOEL: 750 mg/kg (rabbit, oral); 125 mg/kg (dogs, oral)</li> <li>• 500 ppm tolerated for 140 h (6 h/d) in guinea pigs, rabbits and a monkey</li> <li>• Common symptoms of acute toxicity are CNS depression, slight irritation of respiratory tract and histopathologic changes in liver and kidneys</li> <li>• 13-wk inhalation study in both sexes of rats and mice exposed at 0, 94, 187, 373, 748 and 1,500 ppm; lowest effect of 187 ppm in female rats and mice (both sexes) based on decreased Hct values and Hb concentration, (mild) increased cellularity of bone marrow (rats) and respiratory hyaline droplets (rats and mice) (severity was mild)</li> <li>• 6-mo inhalation study in male rats and male rabbits exposed at 98 and 745 ppm: <ul style="list-style-type: none"> <li>○ slight depression of Hct and Hb concentrations and decreased weight gain in rats at 745 ppm</li> <li>○ increased thyroid weights in rats at 98 and 745 ppm</li> <li>○ increased thyroid weights and decreased thyroid hormone in rabbits at 98 and 745 ppm</li> </ul> </li> <li>• 2-yr inhalation study in male and female rats exposed at 100 ppm and 200 ppm showed no pharmacologic or haematologic effects or effects on organ weight: <ul style="list-style-type: none"> <li>○ body weights of female rats slightly less than controls</li> </ul> </li> <li>• Evidence of carcinogenic activity in male and female mice and female rats (2 yr, inhalation): <ul style="list-style-type: none"> <li>○ exposure of male and female rats at 0, 94, 188 or 375 ppm and exposure of male and female mice at 0, 188, 375 or 750 ppm caused increased incidence of mammary gland fibroadenomas and carcinomas in female rats (188 and 375 ppm)</li> <li>○ increased incidence of Harderian gland adenomas and carcinomas in male mice (375 and 750 ppm)</li> <li>○ increased incidence of liver neoplasms and Harderian gland adenomas and carcinomas in female mice (188 and 750 ppm)</li> </ul> </li> </ul>		



Source	Year set	Standard
		<ul style="list-style-type: none"> <li>○ higher incidence of non-neoplastic nose lesions, including effects on nasal cavity and respiratory tract, in male and female mice at all dose levels</li> <li>• Negative results in genotoxic assays</li> <li>• Skin notation not assigned based on lack of evidence in animals that absorption results in systemic injury.</li> </ul> <p>Insufficient data to recommend SEN notation or TLV-STEL.</p>
<b>DFG</b>	<b>2003</b>	<b>Not assigned</b>
Summary of additional data:		
<ul style="list-style-type: none"> <li>• Skin notation based on this dermal penetration rate calculated as 0.6 mg/cm<sup>2</sup>/h:               <ul style="list-style-type: none"> <li>○ related animal test results appear limited</li> </ul> </li> <li>• NOAEC could not be determined for rat or mice from 13-wk inhalation study (described in ACGIH, 2001 above)</li> <li>• No mechanistic explanation for tumour development</li> <li>• MAK not established since not possible to derive NOEL for inhalation exposure; previous MAK of 100 ppm withdrawn due to effects observed at lowest tested concentration of 94 ppm.</li> </ul>		
<b>SCOEL</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>OARS/AIHA</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>HCOTN</b>	<b>NA</b>	<b>NA</b>
No report.		

## Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓ 2016	<ul style="list-style-type: none"> <li>• LD<sub>50</sub>: &gt;2,000 mg/kg (rabbits)</li> <li>• Tumours observed in long-term inhalation studies in rats and mice appear equivocal.</li> </ul>
IARC	✓ 2000	<ul style="list-style-type: none"> <li>• Sufficient evidence for carcinogenicity in experimental animals.</li> </ul>
NTP	✓ 1997	<ul style="list-style-type: none"> <li>• Discussion of 16 d, 13 wk and 2 yr studies in rats and mice (whole-body inhalation exposures); from 13-wk study, lowest effect in (female) mice of 94 ppm based on respiratory hyaline droplets (severity was mild).</li> </ul>
ECHA	✓ 2019	<ul style="list-style-type: none"> <li>• NOAEC = 235 mg/m<sup>3</sup> (94 ppm) for microcytic anaemia and hyperplasia of the bone marrow, citing 13-wk inhalation study (rat only) as described in ACGIH (2001) and DFG (2003)</li> <li>• 2 workers in headlight assembly plant exposed <i>via</i> dermal and inhalation routes for 1–2 mo, developed severe peripheral neuropathy; environmental sampling found exposure at the TLV (value not provided).</li> <li>• DNEL for long-term exposure 20 mg/m<sup>3</sup>.</li> </ul>

**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	NA
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A3
DFG	Carcinogenicity – 3B, H (skin)
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 2B
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:

Dermal LD<sub>50</sub> ≤ 1000 mg/kg:

Dermal repeat-dose NOAEL ≤ 200 mg/kg:

Dermal LD<sub>50</sub>/Inhalation LD<sub>50</sub> < 10:*In vivo* dermal absorption rate > 10%:Estimated dermal exposure at WES > 10%: **yes****insufficient data to assign a skin notation****IDLH**

Is there a suitable IDLH value available?

Yes

## Additional information

Molecular weight:	61.04
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m <sup>3</sup> ; 1 mg/m <sup>3</sup> = Number ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> SCOEL

## Workplace exposure standard history

Year	Standard
Click here to enter year	

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7<sup>th</sup> Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [TLVs® and BEIs® Guidelines section](#) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2003) Nitromethane – 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).

International Agency for Research on Cancer (IARC) (2000) Volume 77, Some industrial chemicals. IARC Monographs on the evaluation of the carcinogenic risk to humans.

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

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

National Toxicology Program (NTP) (1997) NTP-TR-461: Nitromethane.

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