

## TETRANITROMETHANE

**CAS number:** 509-14-8

**Synonyms:** TNM

**Chemical formula:**  $\text{CN}_4\text{O}_8$

### Workplace exposure standard (amended)

**TWA:** —

**STEL:** —

**Peak limitation:** —

**Notations:** —

**IDLH:** —

**Sampling and analysis:** N/A

### Recommendation and basis for workplace exposure standard

This chemical has been nominated for removal from the *Workplace exposure standards for airborne contaminants* due to a lack of evidence that it is used or generated in Australian workplaces or that it presents a potential for legacy exposure. Therefore, a TWA is not recommended.

### Discussion and conclusions

Tetranitromethane (TNM) is used as an oxidizing agent in rocket propellants and explosives, an additive in diesel fuel to increase octane rating and as a reagent for nitration of tyrosine in proteins and peptides. There is lack of evidence that this chemical is used or generated in Australian workplaces or that it presents a potential for legacy exposure.

The critical effects of exposure are ocular and respiratory tract irritation and carcinogenicity.

Workers exposed at unidentified concentrations complained of ocular and respiratory tract irritation and other reports of salivation, coughing, bronchopneumonia, pulmonary oedema and methemoglobinemia noted. Alveolar/bronchiolar adenomas and carcinomas in rats exposed at 2 ppm and in mice at 0.5 ppm are reported in a two-year inhalation study in rats and mice. Both concentrations were the lowest tested. It is genotoxic in microorganisms and in cultured mammalian cells (ACGIH, 2018; DFG, 2006; IARC, 1996; NTP, 2016). This evidence suggest that carcinogenicity may act through a mutagenic mechanism and DFG (2006) note it is a proven genotoxic carcinogen. ACGIH (2018) considered its carcinogenicity as non-classifiable to humans. IARC (1996) classify it as possibly carcinogenic to humans and NTP (2016) state that it is reasonably anticipated to be a human carcinogen.

This chemical has been nominated for removal from the WES list. A TWA is not recommended.

## **Recommendation for notations**

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Based on the data presented, a review of this classification is recommended.

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

There are insufficient data to recommend a skin notation.

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## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>1991</b>	<b>TWA: 1 ppm (8 mg/m<sup>3</sup>)</b>
<b>ACGIH</b>	<b>2001</b>	<b>TLV-TWA: 0.005 ppm (0.04 mg/m<sup>3</sup>)</b>
<p>TLV-TWA recommended to minimise the potential for ocular and respiratory tract irritation and potential respiratory carcinomas reported in rats and mice.</p> <p>Summary of data:</p> <ul style="list-style-type: none"> <li>TLV-TWA based on data from 2 yr animal inhalations studies and evidence of carcinogenicity in rats and mice: <ul style="list-style-type: none"> <li>2 ppm in rats and 0.5 ppm in mice, both lowest tested concentrations, induced alveolar/bronchiolar carcinomas in the two species. No further specific derivation presented</li> </ul> </li> <li>No relevant pharmacokinetic or metabolism evidence.</li> </ul> <p>Human data:</p> <ul style="list-style-type: none"> <li>Workers exposed to unidentified concentrations of TNM complained of ocular and respiratory tract irritation</li> <li>Reports of salivation, coughing, bronchopneumonia, pulmonary oedema and methemoglobinemia (cyanosis) in workers have also been published.</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>Cats exposed for a single 20 min inhalation at ≈10 ppm showed obvious signs of intoxication: <ul style="list-style-type: none"> <li>some of these animals died after 10 d</li> </ul> </li> <li>Exposure for 6 h on 2 consecutive days at 0.1–0.4 ppm caused mild irritation in cats; no other effects observed</li> <li>Groups of 5 male and 5 female rats exposed <i>via</i> inhalation for 6 h/d, 5 d/wk for 14 d at 0, 2, 5, 10, or 25 ppm: <ul style="list-style-type: none"> <li>all rats exposed at 25 ppm died by day 2, reduced survival seen in rats exposed at 10 ppm;</li> <li>pulmonary oedema obvious in rats exposed at 25 ppm</li> </ul> </li> <li>Rats and mice underwent whole-body inhalation exposure for 6 h/d, 5 d/wk to TNM vapour; 0, 2, and 5 ppm for groups of 50 rats of each sex and 0, 0.5, and 2 ppm for groups of 50 mice of each sex: <ul style="list-style-type: none"> <li>alveolar/bronchiolar carcinomas occurring in nearly all rats exposed at 5 ppm; many carcinomas had metastasised to other sites</li> <li>many rats exposed at 5 ppm also had squamous cell carcinomas of the lung (male: 0/50; 1/50; 19/50; female: 0/50; 1/50; 12/50)</li> <li>no neoplastic changes in tissues of nasal passage seen in rats</li> <li>alveolar/bronchiolar neoplasia, primarily carcinomas increased in male and female mice; many carcinomas had metastasised to other sites</li> <li>in male mice, the increases were 12/50 in controls, 27/50 at 0.5 ppm, and 47/50 at 2 ppm</li> </ul> </li> </ul>		

Source	Year set	Standard
		<ul style="list-style-type: none"> <li>in female mice, the increases were 4/49 in controls, 24/50 at 0.5 ppm, and 49/50 at 2 ppm</li> <li>carcinogenic activity appears to be associated with activation of the K-ras oncogene and due to the chronic epithelial irritation mitotic stimulation and resultant hyperplastic response</li> <li>Mutagenic with and without metabolic activation in <i>S. typhimurium</i> strains TA1535, TA97, TA98, TA100, and TA102; and in <i>E. coli</i> WP2 uvrA.</li> </ul> <p>Insufficient data to recommend a skin or sensitiser notation of TLV-STEL.</p>
<b>DFG</b>	<b>2006</b>	<b>Not assigned</b>
<p>No MAK as it is classified as a carcinogenic substance based on evidence of carcinogenicity in rodents and genotoxicity in microorganisms and in cultured mammalian cells.</p> <p>Summary of additional data:</p> <ul style="list-style-type: none"> <li>Malignant tumours induced in the lungs of almost all mice exposed at 2 ppm and rats exposed at 5 ppm; cited by ACGIH (2018)</li> <li>Mutagenic effects observed in the <i>S. typhimurium</i> strains TA1535, TA97, TA102 and TA98 but not in TA1537, a strain which can only be reverted by frameshift mutation; these results show TNM induces mutations by base pair exchange</li> <li>Tested for genotoxic effects in cultured mammalian cells (CHO cells); incubations without rat liver S9 mix, incidence of sister chromatid exchange (SCE) increased in a dose-dependent and reproducible manner; addition of S9 mix prevented this effect</li> <li>Modelled dermal flux of 0.010 mg/cm<sup>2</sup>/h</li> <li>Designated a skin notation as absorption from calculated model indicated increased additional carcinogenic risk from dermal exposure.</li> <li>Studies of absorption, distribution, metabolism and excretion not identified.</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
IARC	✓ 1996	<ul style="list-style-type: none"> <li>Cited same 2 yr inhalation study in rodents as ACGIH (2018) and DFG (2006)</li> <li>Genotoxic in bacteria and cultured mammalian cells. Tumours from tetranitromethane-treated rats and mice had a GC:AT transition in the second base of codon 12 of the K-ras oncogene</li> <li>Possibly carcinogenic to humans.</li> </ul>

Source	Year	Additional information
NTP	✓ 2016	<ul style="list-style-type: none"> <li>Reasonably anticipated to be a human carcinogen based on evidence in rats and mice.</li> </ul>

### Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Yes

Is the chemical carcinogenic with a mutagenic mechanism of action? Yes

**The chemical is a non-threshold based genotoxic carcinogen.**

Is a cancer slope factor or inhalation unit risk value available? No

### Notations

Source	Notations
SWA	—
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A3
DFG	Carcinogenicity – 2, 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?

No, the chemical is a genotoxic carcinogen

### Additional information

Molecular weight:

196.04

Conversion factors at 25°C and 101.3  
kPa:

1 ppm = 8.02 mg/m<sup>3</sup>; 1 mg/m<sup>3</sup> = 0.13 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 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) (2006) Tetranitromethan – MAK value documentation.

International Agency for Research on Cancer (IARC) (1996) Tetranitromethane. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Toxicology Program (NTP) (2016) Tetranitromethane: 14th Report on Carcinogens

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

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