

# TETRAMETHYL SUCCINONITRILE

**CAS number:** 3333-52-6

**Synonyms:** Tetramethylsuccinic acid dinitrile, TMSN

**Chemical formula:** C<sub>8</sub>H<sub>12</sub>N<sub>2</sub>

## Workplace exposure standard (retained)

**TWA:** 0.5 ppm (2.8 mg/m<sup>3</sup>)

**STEL:** —

**Peak limitation:** —

**Notations:** Sk.

**IDLH:** 5 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 (2.8 mg/m<sup>3</sup>) is recommended to protect for headaches and nausea and effects on the central nervous system (CNS) in exposed workers.

## Discussion and conclusions

Tetramethyl succinonitrile (TMSN) is a by-product during the production of vinyl foam and from its use as a polymerisation catalyst in photocopier toner.

Critical effects of exposure are headache, nausea and CNS toxicity that can result in convulsions. Very limited data are available. There are case reports of headaches, nausea, convulsions and coma in workers employed at vinyl chloride foam making plants. Exposure details are not specified and possible exposure to other chemicals may have occurred. It is reported to be a potent convulsant in rodents (ACGIH, 2018). A NOAEL of 1 mg/kg/day is reported for liver effects in both dogs and rats from sub-chronic oral studies (HCOTN, 2002).

Given the limited available data, the TWA of 0.5 ppm (2.8 mg/m<sup>3</sup>) is recommended to be retained to limit effects on the CNS based on the recommendation by ACGIH (2018). The TWA is consistent across the primary sources.

## 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 systemic effects following dermal uptake in animals.

## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>1991</b>	<b>TWA: 0.5 ppm (2.8 mg/m<sup>3</sup>)</b>
<b>ACGIH</b>	<b>2001</b>	<b>TLV-TWA: 0.5 ppm (2.8 mg/m<sup>3</sup>)</b>
<p>TLV-TWA recommended to minimise the potential for headache, nausea, and CNS toxicity.</p> <p>Summary of data:</p> <p>TLV recommend since 1967; no derivation presented.</p> <p>Limited toxicological data are available.</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>• Several workers in a PVC foam plant complained of headaches and nausea; no further information</li> <li>• Report of headaches, nausea, convulsions and coma (no further information) in 7 women and 9 men employed making vinyl foam products: <ul style="list-style-type: none"> <li>○ of the 16 workers, 12 complained of headaches and 5 experienced convulsions;</li> <li>○ presence of TMSN not confirmed and possible exposure to vinyl chloride and other chemicals. No further information.</li> </ul> </li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>• Potent convulsant in rodents</li> <li>• Lethal in rats inhaling 60 ppm for 2–3 h or 6 ppm for 30 h</li> <li>• Overt maternal toxicity in reproductive studies in rats following parenteral injection.</li> </ul> <p>Skin notation recommended based on structural similarity to other dinitriles that can be dermally absorbed causing systemic toxicity and death in animals.</p> <p>Insufficient data to recommend a sensitiser or carcinogenicity notation of TLV-STEL.</p>		
<b>DFG</b>	<b>2001</b>	<b>Not assigned</b>
<p>Insufficient data in humans and animals to derive a MAK.</p> <ul style="list-style-type: none"> <li>• The lowest dermal lethal dose for rabbits with 24 h patch is 79.4 mg/kg.</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>2002</b>	<b>TWA: 0.5 ppm (3 mg/m<sup>3</sup>)</b>
<p>Administrative OEL</p> <p>Summary of additional data:</p>		

Source	Year set	Standard
		<ul style="list-style-type: none"> <li>• 15 male and 15 female rats administered by gavage 0, 1, 3 or 10 mg/kg/d over 90 d; treatment-related morphological changes in the kidney of male and not female rats at all dosage levels: <ul style="list-style-type: none"> <li>○ treatment-related liver changes in male and female rats given 10 mg/kg/d</li> <li>○ absolute and relative liver weights significantly increased in rats exposed to doses of 3 mg/kg/d</li> <li>○ NOAEL of 1 mg/kg/d</li> </ul> </li> <li>• 4 groups of 4 male and 4 female dogs, administered TMSN <i>via</i> capsules (0, 0.3, 1.0 and 3.0 mg/kg/d) for 90 d: <ul style="list-style-type: none"> <li>○ female dogs body weight gain was slightly suppressed</li> <li>○ relative liver weights significantly increased at necropsy in 4/8 dogs (3 female, 1 male) of the highest dose group. No (microscopic) histological effects related to treatment in either liver or kidney found</li> <li>○ authors concluded NOAEL of 1 mg/kg/d</li> </ul> </li> <li>• A recommended HBROEL derived by starting with the NOAEL of 1 mg/kg/d reported in animals: <ul style="list-style-type: none"> <li>○ since workers are exposed for 5 d/wk the NOAEL from a continuous feeding study is adjusted by multiplying with a factor of 7/5, resulting in a NOAEL of 1.4 mg/kg/d</li> <li>○ for differences in caloric demand between rats and humans a scaling factor of 4 is applied</li> <li>○ overall UF of 12 is applied to account for inter- and intraspecies variation and the duration of exposure</li> <li>○ assuming 100% absorption, 70 kg body weight and a breathing volume of 10 m<sup>3</sup> 8 h per working day</li> <li>○ derive a health-based OEL of 0.2 mg/m<sup>3</sup> TWA.</li> </ul> </li> </ul>

## Secondary source reports relied upon

NIL.

## 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	Skin
HCIS	NA
NICNAS	NA
EU Annex	NA

Source	Notations
ECHA	NA
ACGIH	Skin
DFG	H(skin)
SCOEL	NA
HCOTN	—
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

Adverse effects in human case study:

Dermal LD<sub>50</sub> ≤ 1000 mg/kg: **yes**

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%:

**consider assigning a skin notation**

### IDLH

Is there a suitable IDLH value available? **Yes**

### Additional information

Molecular weight:	136.2
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 5.56 mg/m <sup>3</sup> ; 1 mg/m <sup>3</sup> = 0.180 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 checked="" 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
<a href="#">Click here to enter year</a>	

## 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) (2001) Tetramethylsuccinonitril – MAK value documentation.

Health Council of the Netherlands (HCOTN) (2002) Tetramethyl succinonitrile. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/041.

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