TRIMETHYLAMINE

CAS number: 75-50-3

Synonyms: Dimethylmethaneamine, TMA

Chemical formula: C_3H_9N

Workplace exposure standard (retained)

TWA: **10 ppm (24 mg/m^3)**

STEL: **15 ppm (36 mg/m^3)**

Peak limitation: **—**

Notations: **—**

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 10 ppm (24 mg/m^3) and STEL of 15 ppm (36 mg/m^3) are recommended to protect for irritation of the upper respiratory tract (URT), eyes and skin and to reduce the risk of transient visual effects in exposed workers.

Discussion and conclusions

Trimethylamine (TMA) is used as an insect attractant, as a warning agent in natural gas, as a flotation agent and as an intermediate in chemical synthesis. It is a natural decomposition product of nitrogenous plant and animal macromolecules and is widely distributed in animal tissue, especially fish.

The critical effects of exposure are upper respiratory tract (URT), eye and skin irritation and transient vision disturbances.

Transient visual disturbances, referred to as blue veil vison or halovision, are reported in workers exposed to amine vapours including TMA for several hours. No further exposure information is provided. Moderate irritation of the URT occurs in workers exposed at 20 ppm and greater with a NOAEC reported at 8 ppm. Oedema reported in two volunteers following an eight-hour exposure at 9.7 ppm (SCOEL, 2017; AIHA, 2005). Damage to the nasal mucosa that appeared reversible at 75 ppm reported in sub-chronic inhalation studies in rats. A NOAEC of approximately 10 ppm is reported in another rat inhalation study. In humans, it has a highly offensive odour that is apparent at concentrations of less than 1 ppm (ACGIH, 2018). It is analogous with N,N-dimethylethylamine (blue veil vison outcomes) and with cyclohexylamine and dimethylamine (irritation outcomes) each having TWA of 2 ppm (DFG, 2018).

There are inconsistent data and decisions about recommended occupational exposure limits by primary agencies. Based on moderate irritation of the URT in workers at 20 ppm with a NOAEC of 8 ppm and a NOAEC of 10 ppm in a rat inhalation study, the TWA of 10 ppm and STEL of 15 ppm are recommended to be retained. The fact TMA has a highly offensive odour at concentrations greater

than 1 ppm will also likely be a limiting factor for worker exposure. The recommended TWA and STEL are considered protective of the critical effects.

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.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1986***	***TWA: 10 ppm (24 mg/m^3); STEL: 15 ppm (36 mg/m^3)***
No report. Adopted from the ACGIH 1986.		
ACGIH	***2013***	***TWA: 5 ppm (12 mg/m^3); STEL: 15 ppm (36 mg/m^3)***
TLV-TWA recommended to minimise URT, eye and skin irritation. TLV-STEL based on analogy to methylamine recommended to minimise irritation from peak exposures. Summary of data: • TLV-TWA based on results of inhalation tests in animals; no specific derivation provided. • It has an offensive, pungent, fishy, ammoniacal odour and saline taste with an odour threshold reported between 0.2–0.8 ppb; at the TLV-TWA concentration, the odour of trimethylamine is likely sufficiently unpleasant to work under those conditions • TLV-STEL of 15 ppm based on analogy to methylamine, with irritation documented in humans exposed at ≥20 ppm. Human data: • Corrosive to intact human skin when applied as concentrated solution; petechial haemorrhages appeared on the skin even when the solution was washed away with soap and water within minutes of application • Accidental human eye contact with TMA caused corneal epithelial sloughing; the initial damage was followed by prompt healing with no sign corneal or ocular injury within 4–5 d. Animal data: • Groups of rats exposed 6 h/d, 5 d/wk for 2 wk at 0, 75, 250 or 750 ppm TMA vapour: ○ Concentration-dependent degenerative changes in nasal olfactory and respiratory mucosa at all exposure levels, histopathologic examination after 10 d; resolved at end of 2 wk recovery period ○ degeneration of tracheal mucosa reported at 250 and 750 ppm ○ NOAEL not determined, although irritation reported at 75 ppm was considered slight to moderate and of a transient nature • A similar study where rats inhaled 0, 10 or 31 ppm for 7 mo; reported a NOAEC of ≈10 ppm (data and information very limited) • Instillation of single drops of aqueous solutions in animal eyes demonstrated that TMA can produce severe eye irritation and damage, increasing with concentration • No relevant carcinogenicity studies identified; no evidence for mutagenic activity of in *S. typhimurium* strains TA1535, TA1537, TA98 and TA100 could be detected with or without activation.		
DFG	***2018***	***MAK: 2 ppm (4.9 mg/m^3)***
MAK recommended based on evidence of local irritation of the respiratory epithelium of the nose and the blue veil vision observed after exposure to tertiary amines.		

Source	Year set	Standard

Summary of additional data:
• MAK value of 2 ppm based on:
  ○ comparison with N,N-dimethylethylamine (MAK 2 ppm) and blue veil vison outcomes
  ○ analogy with cyclohexylamine and dimethylamine (MAK 2 ppm) and irritation outcome
  ○ 2 wk inhalation study in rats and irritation outcome.
Blue veil vision
• Blue veil vision observed after the exposure of workers to the tertiary amines N,N-dimethylethylamine and triethylamine cannot be excluded for trimethylamine because of its structural similarity with these substances
• Size of the alkyl groups of the amine play a role in the occurrence of blue veil vision; triethylamine has a stronger effect than N,N-dimethylethylamine with regard to this end point
• Trimethylamine has no ethyl groups, but instead three methyl groups at the nitrogen atom; it can therefore be assumed that its effect is weaker than that of N,N-dimethylethylamine, which has a MAK value of 2 ppm
• A MAK value of 2 ppm for trimethylamine would therefore provide protection for blue veil vision.
Local irritation of the respiratory epithelium of the nose
• 2 wk inhalation study in rats (cited by ACGIH, 2018); the lowest tested concentration of 74 ppm is the LOAEC; (different concentrations as cited by ACGIH; however, same study/author):
  ○ using a procedure not described, DFG derive a NAEC of 25 ppm from the LOAEC of 74 ppm
• Irritation of the eyes and mucous membranes occurred in exposed workers at concentrations ≥20 ppm (no further details)
• Workers exposed at 0.1–8 ppm (8-h mean value <5 ppm), as measured by a manufacturer and by a consumer, had no toxic effects (no further details)
• The MAK of 2 ppm for dimethylamine derived on LOAEC of 10 ppm reported in a 2 yr study for minimal effects on the nasal epithelium of mice and rats.		

SCOEL	***2017***	***TWA: 2 ppm (4.9 mg/m^3); STEL: 5 ppm (12.5 mg/m^3)***
Summary of additional data: • No explanation of the OEL derivations are provided • Stimulates the sensory trigeminal nerve endings, causing facial and eye irritation and causes respiratory tract epithelial damage from a direct toxic effect • Moderate URT irritation occurred in workers at ≥20 ppm (exposure time not specified). No additional details provided • Refers to animal studies cited by ACGIH (2018).		
OARS/AIHA	***2005***	***TWA: 1 ppm***
TWA to protect for halovision, olfactory epithelial damage and fetotoxicity. Will not protect for odour related outcomes. Set in1980, revised in 2005. Summary of additional data:		

Source	Year set	Standard
		• Moderate irritation of the upper respiratory system occurred in workers exposed to ≥20 ppm; NOAEC reported to be 8 ppm; no further information • Halovision or blue veil vision reported in workers exposed for several hours to amines vapours including TMA at levels too low to cause discomfort; no further information • NOAEL for developmental effects in mice ranged between 59 and 148 mg/kg/d (no further details).
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

NIL.

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	NA
DFG	NA
SCOEL	NA
HCOTN	NA
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
Insufficient evidence to recommend a skin notation.

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	59.11
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 4.12 mg/m^3; 1 mg/m^3 = 0.243 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* on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2018) Trimethylamine /N,N-Dimethylmethanamine– MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2017) Recommendation from the Scientific Committee on Occupational Exposure Limits for trimethylamine. SCOEL/REC/179.

Occupational Alliance for Risk Science (OARS) (2005) Workplace environmental exposure level – Trimethylamine.