TOLUENE

CAS number: 108-88-3

Synonyms: Methyl-benzene; methacide; methylbenzol; monomethyl benzene; phenyl methane

Chemical formula: C_7H_8

Structural formula:

Workplace exposure standard (amended)

TWA: **20 ppm (75 mg/m^3)**

STEL: **—**

Peak limitation: **—**

Notations: **—**

IDLH: **500 ppm**

Sampling and analysis: The recommended value is readily quantifiable through currently available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 20 ppm (75 mg/m^3) is recommended to protect for adverse neurological and reproductive effects in exposed workers.

The previous STEL is recommended to be withdrawn as there is insufficient evidence to recommend a STEL.

Discussion and conclusions

Toluene is generated during the process of refining crude oil. It is a component of gasoline and rubber. It is also used as a solvent and to produce other compounds such as plastic.

Toluene is a well-studied chemical with evidence of health effects available from animal, human volunteer and epidemiological studies. Critical effects of exposure are CNS and reproductive effects.

Colour vision changes were reported at average toluene concentrations of 36 ppm (135 mg/m^3) measured in breathing zones in a longitudinal study of print workers with an average employment of 18 years (ACGIH, 2018). A calculated arithmetic mean of the available NOAELs from 10 adequate occupational studies was reported as 34 ppm (127.5 mg/m^3) (US EPA, 2005 cited in NICNAS, 2017). An increased incidence of miscarriage in a study of 55 women exposed at a range of 50-150 ppm (187.5–562.5 mg/m^3) was noted by ACGIH (2018). NICNAS (2017) concluded that a TWA of 50 ppm (191 mg/m^3) may not be adequate to mitigate the risk of reproductive toxicity and neurological effects.

A TWA of 20 ppm (75 mg/m^3) by ACGIH (2018) is recommended to protect for adverse neurological effects and reproductive effects in exposed workers. The previous STEL is recommended to be withdrawn as there is a lack of evidence for immediate acute toxicity within ten times of the recommended TWA.

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 not warranted as there is no indication of systemic effects resulting from skin absorption. Skin notation is recommended to be removed.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***2005***	***TWA: 50 ppm (191 mg/m^3); STEL: 150 ppm (574 mg/m^3)***
ACGIH	***2007***	***TWA: 20 ppm (75 mg/m^3)***

TLV-TWA recommended to protect for subclinical changes in blue-yellow colour vision in exposed workers and the potential for miscarriage in exposed female workers (no specific explanation provided on derivation of TLV-TWA).

Summary of data:

Human data:

- Case reports of intentional toluene abuse (2–10 yr) led to a range of CNS symptoms including headaches, abnormal speech, memory loss, cognitive deficits, ataxia, drowsiness, colour vision changes, hearing loss, mild dementia, tremor and loss of smell. These symptoms are linked to diffuse cortical, cerebellar and cerebral atrophy
- WHO estimates exposures at 4,000 ppm for 1 h or 10,000–30,000 ppm for a few min will result in unconsciousness followed by death
- A longitudinal study of rotogravure printers reported colour vision changes in workers (average employment 18 yr) with average toluene concentrations of 36 ppm measured in breathing zones
- Colour vision changes also reported in rubber plant workers with estimated exposures at time of measurement of 42 ppm (29 yr median exposure duration)
- Colour vision changes were not detected in 63 men and 111 women exposed to 46 ppm (no duration provided)
- A miscarriage rate of 2.8 times higher than a non-exposed reference group was reported in a study of 55 women exposed to an average concentration of 88 ppm of toluene (50–150 ppm).

Animal data:

- Some spatial learning and memory effects reported in rats exposed to 80 ppm (5 d/wk, 6 h/d for 4 wk)
- No evidence of carcinogenic activity in rats or mice in lifetime inhalation studies with toluene concentrations <1,200 ppm
- RD_{50}: 3,300–5,300 ppm in respiratory irritation studies (animal species unknown)
- No eye irritation but mild throat irritation in rabbits at 1,100 ppm
- Reversible high frequency hearing loss reported in male rats following inhalation of 1,400–2,000 ppm toluene (8 h/d for 3 d)
- No evidence of toxicity following dermal application of toluene in mice 3/wk for 4 wk, followed by secondary treatment of 3/wk for up to 112 wk
- Two-generation reproductive toxicity tests *via* inhalation reported no adverse effects on fertility, reproductive performance or maternal/pup behaviours during lactation period in males and females at exposures of 0, 100 and 500 ppm toluene (NOAEL). Growth inhibition and variations in foetal body weight and skeleton development in offspring were reported for the 2,000 ppm exposure group
- LD_{50}: 12,000 mg/kg (rats, dermal)

Source	Year set	Standard
• Not mutagenic in *Salmonella, Escherichia coli, Saccharomyces cerevisiae* or *Drosophila melanogaster.* In 2006 the Skin notation was withdrawn based on studies which showed poor skin absorption. Not classified as human carcinogen. Insufficient data to recommend a TLV-STEL or SEN notation.		
DFG	***1995***	***MAK: 50 ppm (190 mg/m^3)***
Recommended MAK established in relation to adverse effects on performance and subjective effects (how a person feels). Summary of data: • LOAEL of ≈60 ppm for subjective effects in humans • Assumes effect at low level exposures are reversible (no value provided) • Persistent behavioural toxic effects not expected after exposure to 50 ppm.		
SCOEL	***2001***	***TWA: 50 ppm (192 mg/m^3); STEL: 100 ppm (384 mg/m^3)***
TWA and STEL recommended to protect for adverse subjective effects and short-term neurobehavioural effects Summary of data: • Suggested that first effects for both short and long-term are found at ≈75 ppm • No effects on psychophysiological functions (not defined) were found in a study examining the effects of repeated exposure of 12 volunteers to 80 ppm for 4.5 h under laboratory conditions • STEL based on the toxicokinetics of toluene in conjunction with experimental data on human neurobehaviour at 80 ppm • A skin notation was recommended, as dermal absorption of liquid toluene may contribute substantially to the total body burden.		
OARS/AIHA	***NA***	***NA***
No report		
HCOTN	***NA***	***NA***
No report		

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	2017	• Not classified as a respiratory irritant • Skin irritation category 2 • Inhalation study on rats exposed to 80 ppm for 6 h/d, 4 d/wk for 4 wk showed adverse neurobehavioural alterations • Reported NOAEL of 25–50 ppm identified for individual neurological effects (no further information) • US EPA (2005) calculated arithmetic mean of 34 ppm using the available NOAELs from 10 occupational studies that they considered adequate • Advised that based on the available data, the current exposure standard of 50 ppm may not be adequate to mitigate the risk of adverse effects • No significant increase in tumours in rats or mice following inhalation or application to the skin • No epidemiological evidence identified of tumours significantly associated with exposure to the chemical.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	No

Notations

Source	Notations
SWA	Skin
HCIS	—
NICNAS	—
EU Annex	NA
ECHA	—
ACGIH	—
DFG	—
SCOEL	Skin
HCOTN	NA
IARC	—
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:	no	
Dermal LD_{50} ≤1000 mg/kg:	no	
Dermal repeat-dose NOAEL ≤200 mg/kg:		
Dermal LD_{50}/Inhalation LD_{50} <10:		
In vivo dermal absorption rate >10%:		
Estimated dermal exposure at WES >10%:		
		a skin notation is not warranted

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	92.14
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m^3; 1 mg/m^3 = 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* on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (1993) Toluene – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2001) Recommendation from the Scientific Committee on Occupational Exposure Limits for toluene. SCOEL/SUM/18

European Chemicals Agency (ECHA) (2016) – Toluene: RMOA Conclusion Document, EC no 203-625-9

International Agency for Research on Cancer (IARC) (1999) Toluene. IARC Monographs on the evaluation of the carcinogenic risk to humans. VOL: 71.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2017) Toluene: Human health tier II assessment – IMAP report.

US National institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life and health concentrations – toluene.