



VINYL TOLUENE

CAS number: 25013-15-4

Synonyms: Methyl styrene, tolyethylene, 3-vinyltoluene, 4-vinyltoluene

Chemical formula: C₉H₁₀

Workplace exposure standard (amended)

TWA: 20 ppm (97 mg/m³)

STEL: 40 ppm (193 mg/m³)

Peak limitation: —

Notations: —

IDLH: 400 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 (98 mg/m³) is recommended to protect for mucous membrane irritation in exposed workers.

A STEL of 40 ppm (196 mg/m³) is recommended to protect for acute mucous membrane irritation in exposed workers.

Discussion and conclusions

Vinyl toluene is used as an intermediate in the manufacture of plastics, coatings and insecticides.

Critical effects of exposure are objectionable odour and eye and upper respiratory tract (URT) irritation. A poorly documented sensory irritation threshold is reported at 50 to 100 ppm in volunteers; in the same study, a nuisance odour at 200 ppm and strong irritation at 400 ppm are reported (ACGIH, 2018; DFG, 2017). Rodents are more sensitive than humans to URT irritation as evidenced in a chronic inhalation study, in which a LOAEC for damage to the nasal epithelium is reported at 100 ppm in rats and 10 ppm in mice (ACGIH, 2018; DFG, 2017). These results are supported by toxicological data for structurally related styrene, which indicate that local enzymatic oxidation produces irritating metabolites in rats, but not in human nasal tissue *in vitro* (DFG, 2017).

Both ACGIH (2018) and DFG (2017) recommend TWA equivalents based on a combination of the vinyl toluene-specific information and by analogy to the toxicological profile of styrene. Due to the recent amendment of the TLV-TWA for styrene to 20 ppm, ACGIH (2018) states the current TLV-TWA for vinyl toluene is under consideration. In view of this information, a TWA of 20 ppm is recommended to protect for mucous membrane irritation in accordance with the evaluation presented by DFG (2017). Severe irritation may be expected at acute exposures within an order of magnitude of this value. Therefore, a STEL of 40 ppm is recommended, which is below the sensory irritation threshold of 50 ppm in humans and supported by the DFG (2017) evaluation.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). No entry for the substance was found in the HCIS database.

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

A skin notation is not recommended based on the available evidence.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 50 ppm (242 mg/m³); STEL: 100 ppm (483 mg/m³)
ACGIH	2001	TLV-TWA: 50 ppm (242 mg/m³); TLV-STEL: 100 ppm (483 mg/m³)
TLV-TWA and TLV-STEL intended to protect for mucous membrane irritation and objectionable odour. Not classifiable as a human carcinogen. Summary of information: Commercial sources are usually mixtures of m- and p-isomers (50–70% and 30–45%, respectively). Toxicological literature for the methyl styrene isomers often does not specify whether a mixture was studied or if the alpha-methyl styrene or the trans-beta-methyl styrene was studied. TLV-TWA based on analogy to styrene. ACGIH states that in view of the recent amendment of the TLV-TWA for styrene to 20 ppm and evidence for higher neurotoxicity of vinyl toluene compared with styrene in humans and animals, the TLV-TWA for vinyl toluene is being reconsidered. Human data: • A volunteer inhalation study is briefly summarised below (no further details provided): ○ irritation of eyes and URT at 400 ppm ○ objectionable odour at 300 ppm ○ strong tolerable odour at 200 ppm ○ irritating odour, but no mucous membrane irritation at 50 ppm ○ no odour at 10 ppm. Animal data: • Increased kidney and liver weights and fatty liver degeneration at 1,250 ppm (rats, 7–8 h/d, 92–100 d): ○ 600 ppm well-tolerated based on haematology, histology and organ weight • Reduced sensory and motor nerve conduction velocity at 100–300 ppm in subchronic inhalation study (rats, 12–21 wk, dose frequency not specified) • No evidence for electrophysiological changes at 50 ppm (rats, 4 h/d, 5 d/wk, 15 wk) • Dose-dependent nephropathy (rats) >160 ppm and pulmonary inflammation at 160 ppm (mice) in subchronic inhalation study with exposure groups 0, 10, 25, 60 and 160 ppm (mice) and 0, 25, 60, 160, 400 and 1,000 ppm (rats) (6 h/d, 5 d/wk, 13 wk): ○ metaplasia of nasal turbinates observed in all exposed mice • Degeneration of nasal epithelium at 100 and 300 ppm (rats) and 10 and 25 ppm (mice) in chronic inhalation study (6 h/d, 5 d/wk, 2 yr): ○ chronic bronchial inflammation also observed in exposed mice ○ no clinical or microscopic evidence for neurotoxicity in either species, which contrasts results of subchronic inhalation study with rats ○ no evidence for carcinogenic activity • Birth defects in offspring at 6 ppm (4 mo) and 6,200 ppm (1 mo) (guinea pigs, no further details provided) • Non-mutagenic <i>in vitro</i> in bacteria and mammalian cells lines with or without metabolic activation and <i>in vivo</i> in <i>D. melanogaster</i>: ○ epoxide metabolites are mutagenic <i>in vitro</i> in bacteria		

Source	Year set	Standard
		55% of IP dose excreted in urine within 6 h (rats); binds liver cytochrome P-450 and forms epoxide metabolites, which are rapidly enzymatically hydrolysed. Insufficient data to recommend notations for skin absorption and sensitisation.
DFG	2016	MAK: 20 ppm (98 mg/m³)
Summary of additional information: Structurally and toxicologically related styrene is oxidised enzymatically in the nasal epithelium of rodents to produce irritating metabolites. Oxidation of styrene does not occur <i>in vitro</i> in human nasal tissue. Therefore, humans are considered less sensitive than rodents to styrene and vinyl toluene. - MAK based on LOAEC of 100 ppm for local irritation reported in chronic inhalation study in rats (also presented in ACGIH, 2018): - NOAEC of 33 ppm extrapolated from experimental data and rounded down to produce MAK of 20 ppm - value not halved due to lower sensitivity of humans to local olfactory effects compared to rats - slight irritation at 200 ppm and only odour perception at 50 ppm for both styrene and vinyl toluene reported in volunteer study (also presented in ACGIH, 2018) and current MAK of 20 ppm for styrene for the same endpoints support the MAK recommendation. DFG considered that this human study is poorly documented and does not meet present-day requirements. However, it gives a qualitative indication of sensory irritation of vinyl toluene corresponding to styrene as similar concentration of styrene were also investigated - UF factor of 2 applied because local irritation is the critical endpoint and calculated a MAK of 20 ppm according to DFG methodology: - value supported by volunteer study that reported only odour perception and no irritation at 50 ppm - Not classified as carcinogen based on negative results in chronic inhalation study in mice and rats - Skin notation not recommended because dermal absorption not expected to contribute to overall body burden regarding exposure at the MAK based on <i>in vitro</i> dermal absorption rate - Sensitiser notation not recommended based on limited negative or equivocal results for sensitisation for styrene and vinyl toluene in guinea pigs. Human data: - NOAEC of 50–100 ppm for sensory irritation in volunteer inhalation study (no further exposure details provided, also presented in ACGIH, 2018): - nuisance odour at 200 ppm and irritation of eyes and nose at 400 ppm - poorly documented study and only used as qualitative indication of sensory irritation 1 report of dermal cross-sensitisation in a subject sensitised to styrene - Dermal penetration rate <i>in vitro</i>: 66.0±29.9 µg/cm²/h (10 min) 104.2±63.0 µg/cm²/h (1 h) Animal data: - LD₅₀: >4,500 mg/kg (rabbits, dermal); no histopathological findings at this concentration		

Source	Year set	Standard
		• LOAEC of 100 ppm (rats) and 10 ppm (mice) for inflammation and hyperplasia of respiratory epithelium reported in chronic inhalation study (6 h/d, 5 d/wk, 2 yr, also presented in ACGIH, 2018): ○ systemic NOAEC: 100 ppm (rats) and 10 ppm (mice) for reduced bw; this effect observed at 300 and 25 ppm, respectively, in each species ○ no evidence for carcinogenicity in either species • Non-mutagenic <i>in vitro</i> in bacteria • Micronucleus formation reported <i>in vivo</i> in mice at IP dose of 200 mg/kg, but not at 100 mg/kg (lowest tested dose): ○ cytotoxic at IP doses of 200–500 mg/kg • Developmental toxicity at 6 ppm (4 mo) and 6,200 ppm (1 mo) in guinea pigs reported in one study (also cited by ACGIH, 2018) incorrectly referenced and not used by DFG in assessment • Other available developmental toxicity data include repeat gavage studies with dose range of 50–600 mg/kg/d (rats, rabbits, GD 6–27) with NOAELs of 150–600 mg/kg/d (highest tested doses): ○ one study did not report a NOAEL based on reduced maternal and foetal body weight at 50 mg/kg/d (lowest tested dose) ○ none of these studies were used in the assessment because the original publications were not available.
SCOEL	NA	NA
No report.		
OARS/AIHA	NA	NA
No report.		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
IARC	✓ 1994	• Vinyl moiety oxidised to epoxide derivative, which can be oxidised further. Saturation of these metabolic pathways occurs at 250 mg/kg (rats) • Induces SCE in human lymphocytes and micronuclei in mice <i>in vitro</i> • Inadequate evidence for carcinogenic activity in humans and lack of evidence for carcinogenicity in animals: ○ overall evaluation concludes that vinyl toluene is not classifiable as human carcinogen (Group 3).
NTP	✓ 1990	• No evidence for carcinogenicity in chronically exposed mice and rats (also presented in ACGIH, 2018; DFG, 2017).
ECHA	* 2020	• No additional information • No hazards identified, no DNELs reported.

Source	Year	Additional information
US NIOSH	✓ 1994	• IDLH based on acute inhalation toxicity data in humans.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Insufficient data

Is the chemical carcinogenic with a mutagenic mechanism of action? No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	—
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	—
ACGIH	Carcinogenicity – A4
DFG	—
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
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 ₅₀ ≤ 1000 mg/kg:	no	
Dermal repeat-dose NOAEL ≤ 200 mg/kg:		
Dermal LD ₅₀ /Inhalation LD ₅₀ < 10:		
<i>In vivo</i> dermal absorption rate > 10%:		
Estimated dermal exposure at WES > 10%:	no	
a skin notation is not warranted		

IDLH

Is there a suitable IDLH value available? Yes



Additional information

Molecular weight:	118.18
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 4.83 mg/m ³ ; 1 mg/m ³ = 0.207 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) (2017) Methyl styrene (vinyl toluene) (all isomers) – MAK value documentation.

European Chemicals Agency (ECHA) (2020) vinyltoluene – REACH assessment.

International Agency for Research on Cancer (IARC) (1994) Some Industrial Chemicals. IARC Monographs on the evaluation of the carcinogenic risk to humans, Volume 60.

National Toxicology Program (NTP) (1990) Toxicology and Carcinogenesis Studies of Vinyl Toluene (Mixed Isomers) (65%-71% meta-isomer and 32-35% para-isomer) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). NTP Toxicity report series No. 375. DHHS (NIH) Pub No 90-2830.

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