# Xylene (o-, m-, p- isomers)

| CAS number: | 1330-20-7, (Mixed isomers)  95-47-6, (o-Xylene)  108-38-3, (m-Xylene)  106-42-3, (p-Xylene) |
| --- | --- |
| Synonyms: | Dimethyl benzene, methyl toluene (mixed isomers),  1,2-dimethylbenzene, o-dimethylbenzene,  o-methyl toluene, 1,3-dimethylbenzene,  1,4-dimethylbenzene, 1,2-xylene, 1,3-xylene,  1,4-xylene, o-xylene, m-xylene, p-xylene |
| Chemical formula: | C8H10 |

Workplace exposure standard (retained)

| TWA: | **80 ppm (350 mg/m3)** |
| --- | --- |
| STEL: | **150 ppm (655 mg/m3)** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **900 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 80 ppm (350 mg/m3) is recommended to protect for eye and upper respiratory tract (URT) irritation and neurological impairment in exposed workers.

A STEL of 150 ppm (655 mg/m3) is recommended to protect for acute eye and URT irritation and neurological impairment in exposed workers.

## Discussion and conclusions

Mixed xylene is present in petrol and aviation fuel and in many petroleum solvents and is used as a solvent in paints and other coatings and in rubber cements.

The critical effects of exposure are eye and URT irritation and neurological impairment.

The toxicity of the individual isomers of xylene and the mixed isomers is reported to be essentially the same by the sources available. Limited data exists about long-term exposure in humans. Irritation of the eyes and URT is reported in human volunteers exposed at 200 ppm mixed xylene for three to five minutes. Inhalation at 100 ppm for five to six hours produces changes in manual coordination, reaction time and slight ataxia in human volunteers. Whereas, controlled inhalation studies in volunteers at 64 to 150 ppm or up to 300 to 400 ppm do not cause neurologic impairment (ACGIH, 2018). Impairment of equilibrium functions are noted in volunteers after exposure to m-xylene at 200 ppm for four hours (DFG, 2001). A NOAEL of 50 ppm and a LOAEL of 100 ppm (the only doses in the study) are reported in a study in rats based on decreased rotarod performance and decreased latency in the paw-lick response in the hot-plate test (US EPA, 2003).

Based on the evidence that 100 ppm for six hours produces neurological effects in human volunteers, the current TWA of 80 ppm is recommended to be retained. Given irritation of the eyes and URT is observed in humans following short exposure, the STEL of 150 ppm is recommended to be retained.

## 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 recommended based on the available evidence.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 80 ppm (350 mg/m3); STEL: 150 ppm (655 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 100 ppm (434 mg/m3); TLV-STEL: 150 ppm (651 mg/m3) |
| TLV-TWA and TLV-STEL recommended for occupational exposure to all isomers (ortho-, meta-and para-) of xylene to minimise the potential for eye and URT irritation.  Summary of data:  Human data:   * Industrial fatalities due to gross inhalation exposure described headache, fatigue, lassitude, irritability and GIT disturbances (nausea, anorexia and flatulence) as the most frequent symptoms among exposed workers * Other symptoms reported in exposed workers include: * adverse effects to the heart, liver, kidneys and nervous system * blood dyscrasias, death from aplastic anaemia * The presence of benzene as an impurity was a confounding factor in most cases of blood disease associated with xylene * Human volunteers exposed at 200 ppm mixed xylene for 3–5 min experienced irritation to the eyes, nose and throat; air concentration of 100 ppm for 8 h considered as tolerable (no further information) * 7 volunteers exposed at 0, 105, 230 or 460 ppm vapour for 15 min, one reported slight light-headedness at 230 ppm * Volunteers in studies on exposure effects on the CNS at 100 ppm vapor for 5–6 h experienced changes in manual coordination, reaction time and slight ataxia. No concentration–response relationship between eyes closed and eyes open ratio for volunteers exposed at 64–400 ppm (no further information) * Exposure can induce hepatic microsomal system responsible for its *in vivo* detoxication * Inadequate evidence for carcinogenicity in humans.   Animal data:   * LD50: 4.3 g/kg (mixed xylenes, rabbits, dermal) * 2 drops of mixed xylenes instilled into rabbit eyes caused slight conjunctival irritation with very slight, transient corneal injury * 9 rats exposed at 690 ppm of mixed xylenes, 8 h/d, 6 d/wk for 110–130 d and 6 rabbits exposed at 1,200 ppm 8 h/d, 6 d/wk for 40 to 50 d (same study): * exposure caused paralysis of hind legs; weight loss; a slight decrease in leukocytes; increases in blood urea, urinary blood, albumin; and hyperplasia of bone marrow in some animals * slight congestion of kidney, liver, heart, adrenal, lung and spleen observed * no further information * No significant changes in body weight or haematological data were reported in animal studies (rat, guinea pig, monkey and dog) exposed to o-xylene for 6 wk at 780 ppm or 78 ppm continuously for 90 d; no further information * In rats and dogs exposed at 180 ppm, 460 ppm or 810 ppm of mixed xylene for 13 wk caused no significant alterations in body weight, haematology, blood chemistry, urinalysis, organ weights or macroscopic and microscopic pathology of either species observed at any of the concentrations tested: * subchronic NOAEL of 810 ppm * Inadequate evidence for the carcinogenicity in experimental animals. |
| DFG 1983/2001 MAK: 100 ppm (440 mg/m3) |
| MAK based on evidence of impairment of equilibrium functions after exposure to concentrations of 200 ppm and literature does not justify lowering the provisional 100 ppm MAK value further.  Summary of additional data:  Human data:   * Available studies on workers exposed occupationally for long periods poorly documented * The function of the vestibular system seen to be impaired in several series of studies with controlled exposure to m-xylene concentrations of 0, 90, 100, 146, 200 or 280 ppm: * exposure at 200 ppm for 4 h caused marked disorders in the equilibrium vestibular system and in the critical flicker fusion threshold (visual defect) * relevance of these studies is difficult to assess because the meaning of the results obtained for the function of the vestibular system not yet determined * regardless, it was sufficient evidence to reduce MAK to 100 ppm provisionally * Effects in volunteers exposed at 200 ppm (n=9) for 4 h twice with an interval of 2 wk between the exposures in a series of experiments included: * body sway not changed significantly * reaction times, tapping speed, critical flicker fusion frequency, nystagmus deviations and other neurotoxic symptoms not markedly changed * Not found to affect the relationship between body sway with closed eyes and body sway with open eyes except at concentrations fluctuating between 120–400 ppm (cited by ACGIH, 2018): * tendency to effect body sway reported at 100 ppm (n=6), but body sway not confirmed at higher concentration of 200 ppm (not significant) * clear lengthening of simple reaction time and choice reaction time detected at 400 ppm * Male and female workers (n=175) occupationally exposed for 7 yr and compared with 241 controls; average level of exposure was 21.3±21.6 ppm (sum of o-xylene 3.0 ppm, m-xylene 11.4 ppm and p-xylene 6.9 ppm). Workers were selected if they were exposed to solvent containing more than 70 %xylene. Maximum average exposure was 175 ppm: * exposed workers reported symptoms during work and in the last 3 mo significantly more often than the controls * reports of irritation of the eyes and nose, a dry throat and slight dizziness as acute symptoms; increased reporting with increasing exposure * long-term symptoms were vomiting, nightmares, anxiety, forgetfulness, concentration difficulties, dizziness after suddenly standing up, loss of appetite and reduced grip strength * Differences between the groups in haematological parameters (haemoglobin, leukocytes) and biochemical parameters not detected * Physical activity has considerable effect on xylene concentrations in blood in humans: * exposure at rest to a xylene concentration of 100 ppm results in steady-state xylene concentration in blood in range between 1–1.5 mg/L * concentration of xylene concentrations in the blood of people exposed to 100 ppm during light exercise are similar to resting conditions during exposures to xylene concentrations between 200–300 ppm. |
| 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 |
| --- | --- | --- | --- |
| US EPA |  | 2003 | * Human volunteers exposed under controlled conditions to concentrations in the range of 200–400 ppm for short time periods (15 min–4 h) have reported symptoms of irritation (watering eyes and sore throat) or neurological impairment (mild nausea, headache) * Rats exposed to 50 or 100 ppm m-xylene alone had statistically significantly increased sensitivity to pain at the end of the 3-mo exposure (latency of the paw-lick response was 8.7 and 8.6 seconds, respectively, vs.12.2 seconds for the controls): * LOAEL is 100 ppm, based on decreased rotarod performance and decreased latency in the paw-lick response in the hot-plate test * NOAEL is 50 ppm. |
| NICNAS |  | 2019 | * No further information. |

### 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 | — |
| HCIS | — |
| NICNAS | — |
| EU Annex | NA |
| ECHA | — |
| ACGIH | Carcinogenicity – A4 |
| DFG | H(skin) |
| 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: | no |  |  | | Dermal LD50 ≤1000 mg/kg: | no |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <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: | 106.16 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 4.34 mg/m3; 1 mg/m3 = 0.231 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*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (1983) Xylene (all Isomers) – MAK value documentation.

Deutsche Forschungsgemeinschaft (DFG) (2004) Xylene (all Isomers) – MAK value documentation.

International Agency for Research on Cancer (IARC) (1999) Xylenes. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2019) Xylenes: Human health tier II assessment – IMAP report.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Xylene (o-, m-, p-isomers).