

**XYLENES****Identity**

Name (parent)	Xylene (technical grade)	o-Xylene	m-Xylene	p-Xylene
UN number	1307	1307	1307	1307
CAS number	1330-20-7	95-47-6	108-38-3	106-42-3
Intervention value (AGW in mg/m ³)	1000	1000	1000	1000
Structure	C ₈ H ₁₀	C ₈ H ₁₀	C ₈ H ₁₀	C ₈ H ₁₀

Occurrence

Chemical state (at 20°C)	Liquid
Physical appearances	Colorless liquid with a sweet odor
Industrial products	Gasoline, paint, adhesives, varnishes, thinners

Physicochemical properties

Molecular weight	106.2	106.2	106.2	106.2
Vapor pressure (mbar at 25°C)	8.0	6.7	8.0	8.2
Octanol/water partition coefficient (log Po/w)	3.1	3.1	3.2	3.2
Water solubility (in g/100 mL at 20°C)	Not soluble in water	Not soluble in water	Not soluble in water	Not soluble in water

Toxicokinetics (parent)

Uptake by inhalation	Pulmonary retention of xylene vapors is 55 - 65 % of the inhaled dose [1].
Uptake by skin absorption	- Liquid exposure: after immersion of one or both hands in m-xylene absorption of m-xylene was 2 µg/cm ² /min in human volunteers [2]; the mean absorption rate in another human experiment was 2.45 µg/cm ² /min, after immersion of both hands in liquid m-xylene for 20 minutes [3]. - Vapor exposure: after exposure of the forearm and hands to m-xylene vapor the flux into the skin of m-xylene was 0.091 µg/cm ² /h (exposure for 20 minutes), 0.072 µg/cm ² /h (exposure for 45 minutes), 0.066 µg/cm ² /h (exposure for 120 minutes) and 0.061 µg/cm ² /h (exposure for 180 minutes) [4]. The contribution of dermal absorption of m-xylene vapors to the body burden was estimated to be 1.8% [5].
Uptake via gastrointestinal tract	Approximately 90 % of xylene is absorbed after ingestion
Distribution	Distribution throughout the body, with high uptake in lipid-rich tissues (e.g. brain, fatty tissue)
Metabolism	Main metabolic pathway xylene: oxidation to methylbenzoic acid and conjugation with glycine to methylhippuric acid [1].
Excretion via lungs	Less than 10 % of absorbed xylene is excreted unchanged via exhalation [1].
Excretion via urine	Main excretion route of absorbed xylene: 90% of absorbed xylene is excreted in urine as methyl hippuric acid [6].
Excretion via feces	Minor excretion route [6]

Toxicodynamics

Mechanisms of toxicity	Neurotoxicity, irritation
Classifications for carcinogenicity	Class 3 [7]
Classifications for reprotoxicity	Possibly higher rate of spontaneous abortions and oligomenorrhea among female workers exposed to xylene [8]
Classifications for sensitizing properties	Contact with xylene can cause immunologic contact urticaria [9]



XYLENES

Biological monitoring

Biomarkers	Methylhippuric acid (MHA) in urine	Xylene in breath	Xylene in blood
Molecular weight	193.2	106.2	106.2
Involved enzymatic metabolism	Conjugation with glycine	-	-
Biological material	Urine	End-exhaled air	Blood
Type of sample	Spot urine	Breath sample	Whole blood
Sampling strategy	< 24 h	1-2 days	< 24 h
Excretion pattern	Bi-phasic elimination: 3.6 hours (1.9-5.3 h) and 30.1 h (16.5-48.4 h) (occupationally exposed painters) [10]; cited in ACGIH [11]; Elimination half-life: approximately 1.5 hours and 20 hours [12]	Biphasic elimination: approximately 1 hour and 20 hours (cited from ACGIH [11])	Biphasic elimination: approximately 1 hour and 20 hours (cited from ACGIH [11])
Materials	Polystyrene universal container (30ml)	Bio-VOC, Tenax TA-tubes	Vacutainer tube with EDTA
Transportation	Within 48 hours at ambient temperature; otherwise at -20°C	At ambient temperature	4 °C
Storage	At -20°C	< 2 h transfer to TENAX; preferably sealed in a plastic bag to avoid contact with ambient air	At -20°C
Stability	> 7 days at ambient temperature < 3 months at -20°C	> 1 month	Not reported
Measurement principle	GC-FID HLPC-UV	GC-FID	Headspace SPME (solid phase microextraction)/GC/FID
Limit of quantification	100 µmol/L (HPLC-UV) (limit of detection) [12]	0.01 nmol/L	o-xylene: 49 pg/mL by headspace SPME/GC/MS (limit of detection) m,p-xylene: 34 pg/mL by headspace SPME/GC/MS (limit of detection) [13]
Aliquot for 1 analysis	2 mL	100 – 300 mL end-exhaled air	2 mL
Recommended adjustments	Use creatinine for urine density adjustment	-	-
Preferred units for expression of	µmol MHA/ mol creatinine	nmol/ L alveolar air	mg/L



XYLENES

results			
Conversion factor	1 mmol/mol = 1.71 mg/g	1 nmol/L = 106.2 ng/L	1 mg/L = $9.42 \cdot 10^{-3}$ mmol/L
Biological exposure value US (BEI) [14]	1.5 g/g creatinine at the end of shift	-	-
Biological Tolerance Value Germany [15]	2000 mg/L urine at the end of exposure or end of shift	-	1.5 mg/L at the end of exposure or end of shift
Reference value	< 10 mg/L [1]	-	< 0.5 µg/ 100 mL [1]
BIOMONECS background in non-smoking m/f adults (based P0.95) [16]	-	m,p-xylene: 0.09 nmol/L o-xylene: 0.20 nmol/L	-
Possible confounders	Active smoking, occupational exposure; metabolism of xylene can be inhibited for about 50% after the consumption of ethanol or the ingestion of aspirin		



XYLENES

References

1. Lauwerys R, Hoet P. Industrial chemical exposure, guidelines for biological monitoring: Lewis publishers; 2001.
2. Engström K, Husman K, Riihimaki V. Percutaneous absorption of m-xylene in man. *Int Arch Occup Environ Health*. 1977 Aug 31;39(3):181-9.
3. Lauwerys RR, Dath T, Lachapelle JM, Buchet JP, Roels H. The influence of two barrier creams on the percutaneous absorption of m-xylene in man. *J Occup Med*. 1978 Jan;20(1):17-20.
4. Kezic S, Janmaat A, Kruse J, Monster AC, Verberk MM. Percutaneous absorption of m-xylene vapour in volunteers during pre-steady and steady state. *Toxicol Lett*. 2004 Nov 2;153(2):273-82.
5. Loizou GD, Jones K, Akrill P, Dyne D, Cocker J. Estimation of the dermal absorption of m-xylene vapor in humans using breath sampling and physiologically based pharmacokinetic analysis. *Toxicol Sci*. 1999 Apr;48(2):170-9.
6. World Health Organization (WHO). Xylenes; Environmental health criteria 190. 1997.
7. International Agency for Research on Cancer (IARC). Agents reviewed by the IARC monographs, volumes 1-99. 2008 12-05
8. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for xylene. 2007.
9. Warner MR, Taylor JS, Leow YH. Agents causing contact urticaria. *Clin Dermatol*. 1997 Jul-Aug;15(4):623-35.
10. Engström K, Husman K, Pfaffli P, Riihimaki V. Evaluation of occupational exposure to xylene by blood, exhaled air and urine analysis. *Scand J Work Environ Health*. 1978 Jun;4(2):114-21.
11. American Conference of Industrial Hygienists (ACGIH). Xylenes (technical or commercial grades). 2001.
12. Health and Safety Laboratory (HSL). Method for methyl hippuric acid (a metabolite of Xylene). 2005.
13. Chambers DM, McElprang DO, Waterhouse MG, Blount BC. An improved approach for accurate quantitation of benzene, toluene, ethylbenzene, xylene, and styrene in blood. *Anal Chem*. 2006 Aug 1;78(15):5375-83.
14. American Conference of Industrial Hygienists (ACGIH). TLVs and BEIs. 2008.
15. Deutsche Forschungsgemeinschaft. List of MAK and BAT values 2008, Commission for the investigation of health hazards of chemical compounds in the work area, Report no. 44. 2008.
16. Scheepers PTJ. Biomarkers of exposure to carcinogens. In: General and applied toxicology. ed: Wiley and Sons. 2008.