



# TOLUENE

## I Identity

Name (parent)	Volatile organic substances
Structure	hydrocarbon

## Occurrence

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

## Physicochemical properties

Molecular weight	~30 - 300
Vapor pressure (mbar at 20°C)	~20-20 000
Octanol/water partition coefficient (log Po/w)	~0-6
Water solubility (in g/100 mL at 20°C)	poor to insoluble

## Toxicokinetics (parent)

Uptake by inhalation	Uptake of toluene is estimated to be 40-60% of the total amount inhaled [1]: in a human experiment with male volunteers exposed for 2 hours to 200 mg/m <sup>3</sup> <sup>2</sup> H <sub>8</sub> -toluene during light exercise the mean uptake was 49.2 ± 4.8 % and ranged from 55.4% (SD: 4.4) during the first 20 minutes to 46.1± 5.5% the last 20 minutes [2].
Uptake by skin absorption	Toluene can be absorbed both as a liquid and a vapor through the skin: The absorption rate of liquid toluene in human forearm skin of nine volunteers was found to range from 14 to 23 mg/cm <sup>2</sup> /hour [3]. The contribution of dermal uptake of toluene vapor to the body burden is 1-2% [4].
Uptake via gastrointestinal tract	Gastrointestinal uptake of toluene is complete [5].
Distribution	Toluene is rapidly distributed, with the highest concentrations in adipose tissue, followed by bone marrow, adrenal glands, kidneys, liver and blood [1].
Metabolism	Approximately 80% of absorbed toluene is converted to benzyl alcohol by cytochrome P-450, oxidized to benzoic acid by alcohol dehydrogenase and the alcohol dehydrogenase system, and is finally conjugated with glycine to hippuric acid [6]. Minor metabolites include <i>ortho</i> - and <i>para</i> -cresol and <i>S</i> -benzyl- <i>N</i> -acetyl-L-cysteine.
Excretion via lungs	20% of absorbed toluene is excreted unchanged via the lungs [1].
Excretion via urine	Main excretion route
Excretion via feces	Negligible excretion route; excretion of pure [ <sup>14</sup> C] toluene in feces of male rats was 0.8 ± 0.2 % (mean ± SEM) [7].

## Toxicodynamics

Mechanisms of toxicity	Neurotoxicity.
Classifications for carcinogenicity	Class 3 [8]
Classifications for reprotoxicity	Possible risk of harm to the unborn child.
Classifications for sensitizing properties	n/a



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## Biological monitoring

Biomarkers	Toluene in whole blood	o-Cresol in urine	Hippuric acid in urine	Toluene in end-exhaled air
Molecular weight	92.1	108.14	179.17	92.1
Involved enzymatic metabolism	-	Cytochrome P450 (CYP1A2, CYP2E1, CYP2B6) [5]	Cytochrome P450 (CYP2E1, CYP2B6, CYP2C8, CYP1A2), alcohol dehydrogenase, Acyl-CoA synthase [5]	-
Biological material	Blood	Urine	Urine	Alveolar air
Type of sample	Whole blood	Spot urine	Spot urine	End-exhaled air
Sampling strategy	< 24 h	< 24 h	< 24 h	1-2 days
Excretion pattern	- Triphasic elimination in blood: 3 min, 40 min and 12.3 h (determined in 9 volunteers exposed to <sup>2</sup> H <sub>8</sub> -toluene during light exercise) [2] - Terminal half-life in blood: 21.2 h (calculated after accidental human poisoning of 2 workers) [9]	- Monophasic elimination with a half-life of 7.4 ± 2.3 h (mean ± SD) (determined in toluene-exposed factory workers) [10]	- Monophasic elimination with a half-life of 74 (female) – 117 (male) minutes (determined in human volunteers) [11]. - Monophasic elimination with a biological half-life of 7.3 ± 3.8 h (mean ± SD) (determined in toluene-exposed factory workers) [10]	- Monophasic elimination of 25 min (determined in human volunteers) [12]. - Terminal half-life in alveolar air: 18.7 h (calculated after accidental human poisoning of 2 workers) [9]
Materials	Syringes containing EDTA or heparin (anti-coagulant) [13]	Polystyrene universal container	Polystyrene universal container	Bio-VOC, Tenax TA-tubes
Transportation	4°C	4°C	4°C	At ambient temperature
Storage	-20°C	5 days at 4°C -20°C	-20°C	< 2 h transfer to TENAX; preferably sealed in a plastic bag to avoid contact with ambient air
Stability	-	At 4°C: 5 days At -20°C: 1 year	At 4 °C: for 1 week At -20°C: for 2 months [14] Ambient temperature: 1 day	> 1 month
Measurement principle	Headspace gas chromatography	GC-MS after hydrolysis and solvent extraction Reversed-phase HPLC-UV [13] GC-MS Capillary GC/ECD	Visible absorption spectrometry [14] Ion chromatography HPLC	Gas chromatography – flame ionization detector (GC-FID) or GC-MS



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Aliquot for 1 analysis	5 mL	5 mL	50 - 100 mL	100 – 300 mL
Limit of quantification	35 ng/L [15] (limit of detection)	< 5 µg/L (limit of detection) [13] 0.05 mg/ L urine (Capillary GC/ECD)	0.002 g/L (limit of detection) [14]	0.01 nmol/L
Recommended adjustments	-	Specific gravity or creatinine	Specific gravity or creatinine	n/a
Preferred units for expression of results	mg/L	µmol o-cresol/ mol creatinine	µmol HA/ mol creatinine	nmol/L alveolar air
Conversion factor	1 mg/L = 0.011 mmol/L 1 mmol/L = 92.1 mg/L	1 µg/L = 5.58 *10 <sup>-3</sup> µmol/L 1 µg/g creatinine = 0.63 µmol/mol creatinine	1 µg/L = 5.58 *10 <sup>-3</sup> µmol/L 1 µg/g creatinine = 0.63 µmol/mol creatinine	1 nmol/L = 92.1 ng/L
Biological exposure value US (BEI)	0.05 mg/L (prior to last shift of workweek) [16]	0.5 mg/L (end-of-shift) [16]	1.6 g/g creatinine (end-of-shift) [16]	-
Biological Tolerance Value Germany [17]	1.0 mg/L (end of exposure or end-of-shift) [17]	3.0 mg/L (end of exposure or end-of-shift; for long-term exposures: after several shifts) [17]	-	-
Reference value	< 5.0 µg/L [1]	< 0.3 mg/g creatinine [1]	< 1.5 g/g creatinine [1]	-
BIOMONECS background in non-smoking m/f adults (based P0.95)	-	-	-	0.61 nmol/L [18]
Possible confounders	Active smoking, occupational exposure  Ethanol and aspirin can prolong the half-life of toluene in the body	Active smoking, occupational exposure  Ethanol and aspirin can prolong the half-life of toluene in the body	<i>Not specific for toluene!</i> Possible interference from diet, e.g. E210 (benzoic acid), that is used as an antioxidant. Active smoking, occupational exposure Ethanol and aspirin can prolong the half-life of toluene in the body	Active smoking, occupational exposure  Ethanol and aspirin can prolong the half-life of toluene in the body
Remark	Other possible biomarkers for toluene in urine: toluene (parent substance), benzyl alcohol, benzylmercapturic acid and benzoic acid (not specific for toluene, possible interference from diet).			



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