

**BENZENE****Identity**

Name (parent)	Benzene
UN number	1114
CAS number	71-43-2
Intervention value (AGW in mg/m ³)	500 (neurotoxicity)
Structure	C ₆ H ₆

Occurrence

Chemical state (at 20°C)	Liquid
Physical appearances	Colorless, highly flammable, nonpolar liquid
Industrial products	Gasoline, product of combustion

Physicochemical properties

Molecular weight	78.1
Vapor pressure (mbar at 20°C)	100
Octanol/water partition coefficient (log Po/w)	2.1
Water solubility (in g/100 ml at 20 °C)	0.18

Toxicokinetics

Uptake by inhalation	Respiratory uptake in a human experiment with 6 volunteers: 46.9% ± 3.7 [1]. Pulmonary retention is approximately 50% [1, 2]
Uptake by skin absorption	Dermal absorption of benzene occurs after exposure to liquid and to vapor : <u>Liquid exposure:</u> In an occupational setting, estimated skin absorption was 22-36 % of total benzene uptake [3]; Experimentally determined permeability coefficient (in vitro study with human skin): 43.84 ± 22.82 cm.h ⁻¹ 10 ⁻⁵ ; absorption of topically administered dose: 0.43 ± 0.23 % [4] <u>Vapor exposure:</u> Uptake of benzene vapors through rat skin exposed to 127,600 mg/m ³ : flux: 0.0191mg/cm ² /hr, permeability coefficient: 0.152 ± 0.006 cm/hr, skin uptake: 0.8% [5]
Uptake via gastrointestinal tract	Not common but has led to intoxications; Gastrointestinal uptake is near to 100% in animal study [2]
Distribution	Accumulation in fatty tissues.
Metabolism	Extensive phase 1 (mainly CYP2E1) and phase 2 metabolism (glutathione-S-transferase) [6].
Excretion via lungs	Fraction eliminated in exhaled air varies between 10 - 50 % [7]. Experiments in human volunteers exposed to 52 – 62 ppm for 4 hours: respiratory excretion 16.8% ± 1.8% [1].
Excretion via urine	Unchanged benzene in urine: 0.1-0.2% [8]. Benzene is mainly excreted in urine after metabolism: phenol (13.2%), catechol (1.6%), hydroquinone (10.2%), S-phenyl mercapturic acid (0.05 – 0.26%) <i>trans,trans</i> -muconic acid (1.9 – 7.3%) [7].
Excretion via feces	n/a

Toxicodynamics

Mechanisms of toxicity	Genotoxicity, neurotoxicity
Classifications for carcinogenicity	IARC 1A (human carcinogen) [9]
Classifications for reprotoxicity	Reproduction toxicity found in animal models: Studies with pregnant animals show that breathing benzene has harmful effects on the developing fetus. These effects include low birth weight, delayed bone formation, and bone marrow damage [2].
Classifications sensitizing properties	n/a



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Biological monitoring

Biomarker	S-phenyl mercapturic acid (SPMA)	trans,trans-muconic acid (ttMA)	benzene (parent)
Molecular weight	239.29	142.11	78.11
Involved enzymatic metabolism	CYP2E1 and GST	CYP2E1 and GST	-
Biological material	Urine	Urine	Alveolar air
Type of sample	Spot urine	Spot urine	End-exhaled breath
Sampling collection	Collect multiple samples over 1-2 days	Collect multiple samples over 1-2 days	Collect multiple samples over 1-2 days; exposure to 10 ppm was detected until 45 h [16]
Excretion pattern	Biphasic elimination: 9.0 ± 4.5 [10] and 45 ± 4 h [11] (determined in workers in the petrochemical industry)	Monophasic elimination: 5.1 ± 2.3 h (determined in workers in the petrochemical industry) [10]	Triphasic elimination: 0.9h, 3h and 15 h [12] and 55-61 min, 3.2-5.9 h and 14-19.7 h [16].
Materials	250 mL polyethylene container with screw cap	250 mL polyethylene container with screw cap	Bio-VOC, Tenax TA-tubes
Transportation	At ambient temperature	At ambient temperature	At ambient temperature
Storage	Stable at 4°C if acidified to pH 2 with 6 M of HCl	Stable at 4°C if acidified to pH 2 with 6 M of HCl	< 2 h transfer to TENAX; preferably sealed in a plastic bag to avoid contact with ambient air
Stability	> 1 month	> 1 month	> 1 month
Measurement principle	Gas chromatography mass spectrometry (GC-MS)	HPLC-UV (absorption at 259 nm)	Gas chromatography – flame ionization detector (GC-FID) or GC-MS
Aliquot for 1 analysis	2 mL	2 mL	100 – 300 mL
Limit of quantification	1 - 5 µg/L (GC-MS)	25 µg/L (HPLC-UV)	0.01 nmol/L (GC-MS)
Recommended adjustments	Density correction by creatinine	Density correction by creatinine	n/a
Preferred units for expression of results	µg SPMA/g creatinine	µg ttMA/g creatinine	nmol/L alveolar air
Conversion factor	1 µg/g = 0.475 µmol/mol	1 µg/g = 0.800 µmol/mol	1 ng/L = 0.0128 nmol/L
Biological Limit Values US (workers)	25 µg SPMA/g creatinine (end of shift) [13]	500 µg ttMA/g creatinine (end of shift) [13]	n/a



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Biological Limit Values Germany (workers) [14]	Benzene in air (mg/m ³) 1.0 2.0 3.0 3.3 6.5 13 19.5	SPMA (mg/g creatinine) 0.010 0.025 0.040 0.045 0.090 0.180 0.270	Benzene in air (mg/m ³) 1.0 2.0 3.0 3.3 6.5 13 19.5	<i>tt</i> -MA (mg/L) - 1.6 - 2 3 5 7	-
BIOMONECS background in non-smoking m/f adults (based on P0.95) [15]	6.5 µg/g (6.5 µg/L) [15]		0.33 µg/g (0.32 µg/L) [15]		0.1 nmol/L [15]
Possible confounders	active smoking		active smoking, bacterial product		active smoking



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References

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