

Benzene or counterparts thereof (the counterparts of benzene are defined by the formula: C_nH_{2n-6})

Definition of causal agent

Benzene is a volatile, colourless, liquid, aromatic hydrocarbon whose vapours are heavier than air, with a boiling-point of 80° C.

Main occupational uses and sources of exposure:

In the past, benzene was widely used as a solvent (in glues, paints, varnishes, lacquers, scouring of metal parts, for dry cleaning and in printing inks); present in amounts of 20% or more in solvent-mixtures in the 50s and 60s; and up to 5% in the 70s. Currently, such uses are strictly regulated (mostly present in solvent mixtures in concentrations of < 0.1 %). Nevertheless the worldwide production of benzene is still growing (Western Europe 10 million tonnes in 2004). It is still present in car fuel (1 to 2% in petrol). It is used in the synthesis of a variety of chemical products (styrene, cumene, cyclohexane, nitrobenzene, chlorobenzene, phenol). Exposure is also possible during the production of benzene via coal tar distillation or from petroleum or when cleaning tanks in which benzene has been stored. It is also a natural part of crude oil and cigarette smoke. Benzene is absorbed by the skin at a rate of 1 mg/cm²/h.

Toxic effects

1. Local effects

Irritant effects

Benzene is an irritant to the skin, eyes and respiratory tract.

See section on *Occupationally caused irritation of the skin and mucous membranes* in Annex I entry nr. 202.

2. Systemic effects

Narcotic effects

Headaches, dizziness, nausea, drowsiness, confusion, unconsciousness, possibly coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- History and study of working conditions showing evidence of acute benzene poisoning;
- and, if available: workplace air monitoring; biological monitoring.

Guide values:

Concentration	time	clinical effects
25 ppm	8 h	no acute clinical symptoms
50-150 ppm	5 h	headache, lassitude, weakness
500 ppm	1 h	vertigo, drowsiness, nausea
7500 ppm	½ h	dangerous to life

Minimum duration of exposure: From a few minutes to a few hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

□ Non-carcinogenic haematological effects

Hypoplasia: thrombocytopenia and/or leucopenia, and/or anaemia

Hyperplasia: thrombocytosis, and/or leucocytosis, and/or erythrocytosis

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by: History and study of working conditions providing evidence of exposure to benzene; and, if available:

Biological monitoring

- blood: benzene
- urine (end of shift sample): t,t-muconic acid, S-phenylmercapturic acid

Workplace air monitoring

Any benzene values found in blood, urine or in terms of the atmospheric concentration require judgment as it should be noted that it is problematic to give a value for the atmospheric concentration and nearly impossible to establish a limit for benzene in blood or the metabolites.

In any event, exposure levels well above current standards and indicating poor control of exposure in the workplace, are therefore likely to have a role in causing ill-health (See section on ***Use of Airborne Occupational Exposure Limits*** in the ***Preface***).

Minimum duration of exposure: A few days are sufficient to cause depression of the bone marrow when exposure takes place at high atmospheric concentrations (160 mg/m³) (> 50 ppm). One month for other haematological effects.

Maximum latent period:

- One year for medullary hyperplasia.
- One month for medullary depression.

Leukaemia

The most common form is acute myeloblastic leukaemia. The relationship between exposure to benzene and development of various other forms of leukaemia or non Hodgkin lymphomas continues to be investigated (See section on ***Occupational cancers*** in the ***Preface***).

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
History and study of working conditions providing evidence of excessive exposure to benzene (both by inhalation and skin absorption); and, if available:

Biological monitoring

- blood: benzene > 5 µg/l;
- urine (end of shift sample) t,t-muconic acid > 2 mg/l, S-phenylmercapturic acid >45 µg/g creatinine.

Workplace air monitoring

- Guide values (for previous exposures): atmospheric concentration > 1 ppm:

Minimum duration of exposure: Six months unless there are antecedents of medullary aplasia.

Maximum latent period: Does not apply.

Induction period: Five years.

☐ Effects on reproduction

Benzene is mutagenic to germ cells. See document on reproductive risks from occupational exposures.

Counterparts of benzene

Definition of causal agent

The most important counterparts of benzene are toluene, xylene and ethylbenzene. Toluene (methylbenzene) boils at 110.6 °C, it is volatile and easily flammable at ambient temperature and pressure. The technical product may contain small amounts of benzene, in the past up to 25%. Xylene (dimethylbenzene) exists in three isomeric forms: ortho, meta and para (boiling point 144.4, 139.1, 138.3° C). Technical grade xylene contains a mixture of these isomers and also some ethylbenzene (boiling point 136.2° C). All these counterparts of benzene are colourless liquids with an aromatic, sweet gasoline-like odour.

Main occupational uses and sources of exposure:

Toluene is mainly used in the production of benzoic acid, benzaldehyde, explosives and many other organic compounds; as a solvent for paints, lacquers, adhesives, etc; petrol additive; extraction agent.

Xylene is widely used as a solvent and thinner for paints and varnishes, often in combination with other organic compounds and as a solvent in glues and printing inks.

Ethylbenzene is used for the production of styrene, as solvent in paints and lacquers and in the rubber and chemical manufacturing industries. It is found in crude oils and combustion products.

Toluene; xylene and ethylbenzene are all absorbable through the skin.

Toxic effects

1. Local effects

Irritant effects

All these products may irritate the skin, eyes, and respiratory tract, especially ethylbenzene. See section on *Occupationally caused irritation of the skin and mucous membranes* in Annex I entry nr. 202.

2. Systemic effects

Acute

Headache, dizziness, nausea, drowsiness, weakness, confusion, unconsciousness and possibly coma, memory loss, nausea, hearing and colour vision loss. Liver damage at high solvent levels may occur.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

- History and study of working conditions providing evidence of acute exposure, and if available:
- Biological monitoring
- Toluene: toluene in blood, o-cresol in urine;
- Xylene: xylene in blood, methylhippuric acid in urine;
- Ethylbenzene: 2-, and 4-ethylphenol or mandelic acid plus phenylglyoxylic acid.
- Workplace air monitoring

Guide values

toluene

2.5 ppm		odour threshold
100 ppm	8 h	no symptoms, very mild headache possible
200 ppm	8 h	mild irritant effects
400 ppm	8 h	irritation, incoordination
800 ppm	3 h	pronounced nausea
4000 ppm	1 h	narcosis

xylene

1 ppm		odour threshold
100 ppm	4 h	no effect on reaction time
200 ppm	4 h	irritant effects, prolonged reaction time, impairment of vestibular and visual function
300 ppm	2 h	performance decrement (decrements in psychometric tests such as memory span and choice reaction time)
700 ppm	1 h	dizziness

Minimum duration of exposure: From a few minutes to a few hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

3. Chronic effects

- See Annex I entry nr. 135 on *Encephalopathies due to organic solvents which do not come under other headings.*
- High chronic toluene exposure may induce liver enlargement.
- There is inadequate evidence in humans for the carcinogenicity of ethylbenzene.
- Toluene in air concentrations about 100 ppm is mutagenic to germ cells.