

## **Aromatic amines or aromatic hydrazines or halogenated, phenolic, nitrified, nitrated or sulfonated derivatives thereof**

### **Definition of causal agent**

Aromatic amines are chemical compounds derived from aromatic hydrocarbons by the replacement of at least one hydrogen atom by an amino group (-NH<sub>2</sub>).

Most common compounds: aniline, aminophenol, 4-aminodiphenyl, 2-naphthylamine, toluidine, 4,4-diaminodiphenyl-methane (MDA), benzidine, phenylendiamine.

### ***Main occupational uses and sources of exposure:***

Synthesis of dyes and pigments; used as intermediates in the manufacture of isocyanates; accelerators and anti-oxidants in the rubber industry; pharmaceutical industry; production of herbicides. The production and use of the following aromatic amines have been banned in the EU, according to Council Directive 88/364/EEC: 2-naphthylamine, 4-aminobiphenyl, benzidine, 4-nitrodiphenyl and their salts.

### **Toxic effects**

Most of the aromatic amines are able to penetrate the intact skin.

#### *1. Local effects*

##### **☐ Irritant effects**

Aromatic amines can irritate the skin, eyes and upper respiratory tract.

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

##### **☐ Allergic effects**

Some aromatic amines induce hypersensitivity in the skin and respiratory tract, *e. g.*: p- (m-) phenylenediamine, nitroanilines, 2-aminophenol.

#### *2. Systemic effects*

##### *Acute*

##### **☐ Haematological disorders**

Methaemoglobinaemia

At methaemoglobin levels > 10%, cyanosis occurs

At methaemoglobin levels > 20 to 25%, hypoxia occurs

At higher methaemoglobin levels: low blood pressure, headache, and nervous system dysfunction.

##### *Haemolytic anaemia*

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Presence of HEINZ bodies in red blood cells.

***Exposure criteria:***

*Minimum intensity of exposure:*

Occupational exposure confirmed by:

- history and study of working conditions providing evidence of repeated acute or intense exposure to aromatic amines (taking into account the possibility of absorption via the skin)

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

*Maximum latent period:* Several days.

**□ Liver effects**

Most occupational over-exposures with aromatic amines lead to transient liver function abnormalities. Disorders of the liver ranging from reversible functional abnormalities to severe atrophy. Jaundice occurred in cases of ingestion of MDA.

*Chronic*

**□ Cancer of the bladder**

Cancer of the bladder (and, to some extent, cancer of the efferent urinary passages) resulting from prolonged exposure to certain aromatic amines, especially benzidine, 2-naphthylamine, 4-aminodiphenyl, o-toluidine and others. To some extent the risk is dependent upon the individual speed of metabolic acetylation of these compounds; persons with a slower acetylation rate have a higher risk than those with faster acetylation.

***Exposure criteria:***

*Minimum intensity of exposure:* Occupational exposure confirmed by:

- history and study of working conditions providing evidence of prolonged/repeated exposure to the above mentioned aromatic amines (taking into account the possibility of absorption via the skin)

*Minimum duration of exposure:* One year

*Minimum induction period:* 10 years

*Maximum latent period:* Not known

See section on ***Occupational cancers*** in the **Preface**.