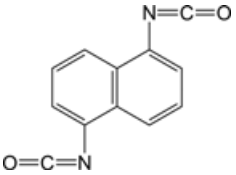
1,5-Naphthylene diisocyanate

BLW (2007)	**Not established** Sampling time: end of exposure or end of shift
Synonym	1,5-diisocyanato naphthalene
CAS number	3173-72-6
Molecular formula	$C_{12}H_6O_2N_2$
Structural formula	
Molecular weight	210.19
Melting point	126.9 °C
Boiling point at 1 013 hPa	167 °C
Vapour pressure at 20 °C	< 0.9 hPa
1 ppm = 8.736 mg/m³	1 mg/m³ = 0.114 ml/m³

MAK value	**Not established**
Peak limitation	–
Absorption through the skin	–
Sensitization (1975)	Sa
Carcinogenicity (2004)	Carcinogen Category 3 B
Prenatal toxicity	–
Germ cell mutagenicity	–

1,5-naphthylene diisocyanate is an aromatic diisocyanate with a very low vapour pressure. It is mainly used in the automobile industry in the production of polyurethane elastomers and synthetic rubber. In its pure and technical forms it is a solid

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substance whose effects are comparable to those of diphenylmethane-4,4′-diisocyanate.

At the workplace 1,5-naphthylene diisocyanate can occur in aerosol and vapour form.

1 Metabolism and Toxicokinetics

For metabolism and toxicokinetics the reader is referred to the MAK documentation (Greim 2000, translated; Greim 2004, translated; Henschler 1975, translated).

2 Critical Toxicity

1,5-naphthylene diisocyanate has a pronounced irritant effect on skin and mucous membranes (Greim 1995, translated). As regards other toxic effects, only a few reports on investigations with occupationally exposed persons are available. In a study with 23 workers exposed to average 1,5-naphthylene diisocyanate concentrations of 0.002 to 0.007 mg/m^3, indications of irritant effects in the respiratory tract were described. Other lung function parameters were unchanged. The induction of asthmatic symptoms typical for diisocyanates ("isocyanate asthma") has only rarely been described for 1,5-naphthylene diisocyanate.

In 3 workers with symptoms of asthma, the bronchial provocation test with 1,5-naphthylene diisocyanate was positive. A further case of respiratory sensitization has been described (Greim 1995, translated). In 4 of 5 persons with workplace-related asthma and in one person with allergic alveolitis similar reactions could be induced by inhalation of 10 ppb 1,5-naphthylene diisocyanate (Baur et al. 2001). Also, in a female worker aged 33 years, allergic asthma was diagnosed. This was attributed to exposure to 1,5-naphthylene diisocyanate (Baur et al. 2000). Investigations on the skin sensitization potential are not available (Greim 1995, translated).

Neither inhalation nor oral studies on the carcinogenicity of 1,5-naphthylene diisocyanate are available. 1,5-diaminonaphthalene, the metabolite of 1,5-naphthylene diisocyanate, has shown genotoxicity and carcinogenic effects in an animal study. As no data on the extent of hydrolytic formation of 1,5-diaminonaphthalene after absorption of 1,5-naphthylene diisocyanate were available, 1,5-naphthylene diisocyanate was classified in carcinogen category 3B and the MAK value was withdrawn (Greim 2004, translated). To avoid deterioration in the lung function of exposed workers it was recommended not to exceed a mean exposure level of 0.05 mg/m^3 and to limit exposure peaks to 0.1 mg/m^3 (Greim 2004, translated).

3 Exposure and Effects

In one study, 15 workers exposed to 1,5-naphthylene diisocyanate were investigated. The person-related 1,5-naphthylene diisocyanate concentrations were between 0.2 and 15 µg/m³ (median: 3 µg/m³) and the 1,5-diaminonaphthalene values in urine were 0.7–81 µg/l (median: 8.4 µg/l) with a detection limit of 0.1 µg/l. A significant correlation between the concentrations of 1,5-diaminonaphthalene in urine and the concentrations of 1,5-naphthylene diisocyanate in the air was found (Sennbro et al. 2006). If one takes these correlation data as a basis, the concentration of 50 µg 1,5-naphthylene diisocyanate/m³ recommended in the MAK documentation would correspond to a 1,5-diaminonaphthalene concentration of 137 µg/l urine.

From 1996 to 2005, 1 974 persons routinely working with 1,5-naphthylene diisocyanate were subjected to occupational medical health surveillance in accordance with Regulation G 27. Among other parameters, 1,5-diaminonaphthalene in urine and specific IgE in serum were determined. The mean 1,5-diaminonaphthalene concentration in 1 974 urinalyses was 8.1 µg/l and the concentration was above the 1,5-diaminonaphthalene detection limit of 5 µg/l in 181 samples. The 1,5-diaminonaphthalene concentration was below 10 µg/l urine in 116 persons. 1,5-diaminonaphthalene values of > 10 to < 100 µg/l could be found in 79 workers, and 1,5-diaminonaphthalene values of ≥ 100 µg/l with a maximum 1,5-diaminonaphthalene value of 2 000 µg/l in 37 workers (Leng 2005 b). The investigation of the specific IgE to 1,5-naphthylene diisocyanate revealed increased values (> 350 kU/l or > 2.0 RU) in 15 cases, thus providing an indication for sensitization. In this case, the IgE finding (Leng 2005 a) did not correlate with the concentration of 1,5-diaminonaphthalene in urine (Leng 2005 b).

4 Selection of Indicators

1,5-diaminonaphthalene in urine can be used as dose marker for 1,5-naphthylene diisocyanate. The biological half-life is about 2 hours (Creely 2006).

In addition, determination of the specific IgE as indicator for 1,5-naphthylene diisocyanate sensitization in the form of a type I allergy is possible.

5 Methods

A method for biological monitoring of aromatic amines, which can also be used for the determination of 1,5-diaminonaphthalene, has been published by the Working Group “Analyses of Biological Materials” (Lewalter et al. 1994, translated).

6 Background Exposure

Occupational medical investigations have shown that in workers without exposure to 1,5-naphthylene diisocyanate no 1,5-diaminonaphthalene is found at a detection limit of 5 µg/l urine (Leng 2005 b).

7 Evaluation

According to Sennbro et al. (2006), the maximum concentration of 50 µg/m³ recommended in the MAK documentation corresponds to a 1,5-diaminonaphthalene concentration of 137 µg/l urine.

Due to the very limited data and as no correlation between health effects and the concentration of 1,5-diaminonaphthalene in the urine has been found in occupational medical cross-sectional studies

the derivation of a "Biologischer Leitwert" (BLW) is not possible at present.

Sampling time: end of exposure or end of shift.

The derivation of exposure equivalents for carcinogenic substances (EKA) is also not possible due to the limited database.

8 Interpretation

To assess possible sensitization, the determination of 1,5-naphthylene diisocyanate-specific IgE is to be recommended; values of > 350 kU/l (radioallergosorbent) or of > 2.0 RU (RAST) are considered to be positive (indicating a sensitization).

9 References

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