[redacted]

1. Chemical and Physical Data

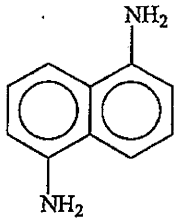
1.1 Synonyms and trade names

Chem. Abstr. Services Reg. No.: 2243-62-1

Chem. Abstr. Name and IUPAC Systematic Name: 1,5-Naphthalenediamine

Synonyms: 1,5-Diaminonaphthalene; 1,5-naphthylenediamine

1.2 Structural and molecular formulae and molecular weight



$C_{10}H_{10}N_2$ Mol. wt: 158.2

1.3 Chemical and physical properties of the pure substance

From Weast (1979), unless otherwise specified

(a) Description: Colourless crystals (Hawley, 1977)

(b) Boiling-point: Sublimes

(c) Melting-point: 190°

(d) Density: 1.4

(e) Solubility: Soluble in hot water, ethanol and diethyl ether; very soluble in chloroform, hot ethanol and hot diethyl ether

(f) Spectroscopic data: Infra-red and ultra-violet spectral data have been reported (Sadtler Research Laboratories, Inc., undated).

1.4 Technical products and impurities

No data were available to the Working Group.

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(a) Production

1,5-Naphthalenediamine can be prepared by the reduction of 1,5-dinitronaphthalene (Sandridge & Staley, 1978) or by ammonolysis of 1,5-dihydroxynaphthalene. Both methods are believed to be used for its commercial production in Japan.

1,5-Naphthalenediamine is believed to be produced by two companies in the Federal Republic of Germany. It has been produced commercially in Japan since 1957; in 1979, two companies produced an estimated 50 thousand kg.

No evidence was found that 1,5-naphthalenediamine has ever been produced in commercial quantities in the US. Two thousand kg were imported through principal US customs districts in 1979 (US International Trade Commission, 1980).

(b) Use

1,5-Naphthalenediamine is believed to be used almost exclusively as an intermediate for the manufacture of 1,5-naphthalene diisocyanate and organic dyes. In Japan, an estimated 75% is consumed in the production of the isocyanate and 25% in dye synthesis.

1,5-Naphthalene diisocyanate, the subject of an earlier monograph (IARC, 1979), is used in Japan and western Europe in the production of polyurethane elastomers. The Society of Dyers & Colourists (1971) reports that 1,5-naphthalenediamine can serve as an oxidation base and that one dye can be prepared from it. No evidence was found that it is presently used commercially in these two applications. The nature of the dyes presently being produced in commercial quantities from 1,5-naphthalenediamine is not known.

2.2 Occurrence

1,5-Naphthalenediamine has not been reported to occur as a natural product. No data on its occurrence in the environment were available to the Working Group.

2.3 Analysis

An IARC manual (Egan *et al.*, 1981) gives selected methods for the analysis of aromatic amines. No information on quantitative methods of analysis for 1,5-naphthalenediamine were available to the Working Group.

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals

Oral administration

Mouse: Groups of 50 male and 50 female B6C3F$_1$ mice, approximately seven weeks of age, were fed diets containing 1000 or 2000 mg/kg 1,5-naphthalenediamine (probably no more than 89% pure, with at least one unspecified impurity detected by thin-layer chromatography) for 103 weeks. The doses were selected on the basis of a range-finding study [see section 3.2(*a*)]. Groups of 50 mice of each sex served as matched controls. All animals in the study received food and water *ad libitum* and all were treated for parasites with 3 g/L piperazine adipate added for three days per week to the drinking-water for two weeks prior to treatment with the test chemical. The observation periods were 105-106 weeks for treated mice and 109 weeks for controls. There was no significant association between dose of 1,5-naphthalenediamine and mortality in animals of either sex; 58-82% of treated mice and 60-66% of controls survived the observation period. Statistically significant increases in tumour incidence were observed for the following neoplasms: (a) a dose-related increase ($P = 0.005$) in C-cell carcinomas of the thyroid gland in females: controls, 0/44; low-dose, 1/49; high-dose, 6/45 ($P = 0.014$); (b) dose-related increases ($P < 0.001$ and $P = 0.003$) in neoplasms of the thyroid gland (follicular-cell adenomas, papillary adenomas and papillary adenomas plus papillary cystadenomas) in 0/38 male controls, 8/46 low-dose males ($P = 0.006$), 16/43 high-dose males ($P < 0.001$), 2/44 female controls, 17/49 low-dose females ($P < 0.001$) and 14/45 high-dose females ($P = 0.001$); (c) an increase in hepatocellular carcinomas in females: controls, 1/46; low-dose, 25/49 ($P < 0.001$); high-dose, 16/46 ($P < 0.001$); and (d) an increase in alveolar/bronchiolar adenomas and carcinomas in females: controls, 0/49; low-dose, 10/48 ($P = 0.001$); high-dose, 5/46 ($P = 0.024$) (National Cancer Institute, 1978).

Rat: Groups of 50 male and 50 female Fischer 344 rats, approximately seven weeks of age, were fed diets containing 500 or 1000 mg/kg 1,5-naphthalenediamine (same sample as used above) for 103 weeks. The doses were selected on the basis of a range-finding study [see section 3.2(*a*)]. Groups of 25 rats of each sex served as matched controls. All animals under study received food and water *ad libitum,* and all were treated for parasites with piperazine adipate added for three days to the drinking-water (followed by three days of plain tap-water and three subsequent days of piperazine adipate) two weeks prior to treatment with the test chemical. The observation periods were 106-107 weeks for treated rats and 109-110 weeks for controls. There was no significant association between dose of 1,5-naphthalenediamine and mortality of animals of either sex: 74-80% of treated rats and 64-68% of controls survived the observation period. A statistically significant, dose-related increase ($P = 0.003$) in the incidence of adenomas plus carcinomas of the clitoral gland was observed: controls, 1/24; low-dose, 3/50; high-dose, 13/50 ($P = 0.021$) (National Cancer Institute, 1978). [The Working Group noted that the increase in the incidence of clitoral gland tumours was only marginally significant, and that histological section of this organ was performed only when it showed gross abnormality.]

3.2 Other relevant biological data

(a) Experimental systems

Toxic effects

No LD_{50} values were available to the Working Group.

In eight-week subchronic feeding studies, male and female Fischer 344 rats and $B6C3F_1$ mice received up to 3.0% 1,5-naphthalenediamine in the diet. Some deaths were observed in treated groups fed 0.3% or more. Mean body weight gain was depressed by 3-22%. No compound-related lesions were observed in chronic studies with 1,5-naphthalenediamine in rats and mice (highest dose, 0.1% in rats and 0.2% in mice) (National Cancer Institute, 1978).

Effects on reproduction and prenatal toxicity

No data were available to the Working Group.

Absorption, distribution, excretion and metabolism

No data were available to the Working Group.

Mutagenicity and other short-term tests

1,5-Naphthalenediamine (same sample as used in the carcinogenicity tests) was mutagenic to *Salmonella typhimurium* strain TA100 without metabolic activation (Dunkel & Simmon, 1980).

(b) Humans

No data were available to the Working Group.

3.3 Case reports and epidemiological studies of carcinogenicity in humans

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Experimental data

1,5-Naphthalenediamine (technical grade) was tested in one experiment in mice and in one experiment in rats by dietary administration. It produced adenomas of the thyroid in male mice and carcinomas and adenomas of the thyroid and lungs and carcinomas of the liver in female mice. The experiment in rats was inadequate for evaluation.

1,5-Naphthalenediamine (technical-grade) was mutagenic to *Salmonella typhimurium.*

4.2 Human data

1,5-Naphthalenediamine has been produced commercially since at least 1957. Its use as an intermediate in the manufacture of 1,5-naphthalene diisocyanate and of dyes could result in occupational exposure.

No case report or epidemiological study was available to the Working Group.

4.3 Evaluation

There is *limited evidence* for the carcinogenicity of 1,5-naphthalenediamine in experimental animals.

No evaluation of the carcinogenicity of 1,5-naphthalenediamine to humans could be made.

5. References

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