TABLE 5

ANALYSES OF THE INCIDENCE OF PRIMARY TUMORS AT
SPECIFIC SITES IN MALE MICE TREATED WITH 1,5-NAPHTHALENEDIAMINE[a]

TOPOGRAPHY:MORPHOLOGY	CONTROL	LOW DOSE	HIGH DOSE
Lung: Alveolar/Bronchiolar Carcinoma[b]	2/39(0.05)	3/46(0.07)	0/45(0.00)
P Values[c]	N.S.	N.S.	N.S.
Relative Risk (Control)[d]	---	1.272	0.000
Lower Limit	---	0.153	0.000
Upper Limit	---	14.686	4.478
Weeks to First Observed Tumor	109	82	---
Lung: Alveolar/Bronchiolar Adenoma or Alveolar/Bronchiolar Carcinoma[b]	4/39(0.10)	9/46(0.20)	2/45(0.04)
P Values[c]	N.S.	N.S.	N.S.
Departure from Linear Trend[e]	P = 0.037	---	---
Relative Risk (Control)[d]	---	1.908	0.433
Lower Limit	---	0.582	0.041
Upper Limit	---	7.882	2.871
Weeks to First Observed Tumor	109	82	105
Hematopoietic System: Malignant Lymphoma[b]	13/39(0.33)	14/47(0.30)	5/49(0.10)
P Values[c]	P = 0.007(N)	N.S.	P = 0.008(N)
Relative Risk (Control)[d]	---	0.894	0.306
Lower Limit	---	0.448	0.094
Upper Limit	---	1.817	0.829
Weeks to First Observed Tumor	100	82	95

TABLE 5 (CONTINUED)

TOPOGRAPHY:MORPHOLOGY	CONTROL	LOW DOSE	HIGH DOSE
Liver: Hepatocellular Carcinoma[b]	12/39(0.31)	10/45(0.22)	7/43(0.16)
P Values[c]	N.S.	N.S.	N.S.
Relative Risk (Control)[d]	---	0.722	0.529
Lower Limit	---	0.318	0.198
Upper Limit	---	1.620	1.306
Weeks to First Observed Tumor	86	88	105
Liver: Hepatocellular Carcinoma or Hepatocellular Adenoma[b]	12/39(0.31)	13/45(0.29)	13/43(0.30)
P Values[c]	N.S.	N.S.	N.S.
Relative Risk (Control)[d]	---	0.939	0.983
Lower Limit	---	0.453	0.473
Upper Limit	---	1.981	2.071
Weeks to First Observed Tumor	86	88	105
Thyroid: C-Cell Carcinoma[b]	0/38(0.00)	0/46(0.00)	4/43(0.09)
P Values[c]	P = 0.017	N.S.	N.S.
Relative Risk (Control)[d]	---	---	Infinite
Lower Limit	---	---	0.825
Upper Limit	---	---	Infinite
Weeks to First Observed Tumor	---	---	105

TABLE 5 (CONCLUDED)

TOPOGRAPHY:MORPHOLOGY	CONTROL	LOW DOSE	HIGH DOSE
Thyroid: C-Cell Carcinoma or C-Cell Adenoma[b]	0/38(0.00)	2/46(0.04)	4/43(0.09)
P Values[c]	P = 0.044	N.S.	N.S.
Relative Risk (Control)[d]	---	Infinite	Infinite
Lower Limit	---	0.246	0.825
Upper Limit	---	Infinite	Infinite
Weeks to First Observed Tumor	---	105	105
Thyroid: Papillary Adenoma, Follicular-Cell Adenoma, or Papillary Cystadenoma NOS[b]	0/38(0.00)	8/46(0.17)	16/43(0.37)
P Values[c]	P < 0.001	P = 0.006	P < 0.001
Relative Risk (Control)[d]	---	Infinite	Infinite
Lower Limit	---	1.905	4.523
Upper Limit	---	Infinite	Infinite
Weeks to First Observed Tumor	---	105	98

[a]Treated groups received doses of 0.1 or 0.2 percent in feed.

[b]Number of tumor-bearing animals/number of animals examined at site (proportion).

[c]The probability level for the Cochran-Armitage test is given beneath the incidence of tumors in the control group when P < 0.05; otherwise, not significant (N.S.) is indicated. The probability level for the Fisher exact test for the comparison of a treated group with the control group is given beneath the incidence of tumors in the treated group when P < 0.05; otherwise, not significant (N.S.) is indicated. For both Cochran-Armitage and Fisher exact tests a negative designation (N) indicates a lower incidence in the treated group(s) than in the control group.

[e]The probability level of the test for departure from linear trend is given beneath the control group when P < 0.05.

TABLE 6

ANALYSES OF THE INCIDENCE OF PRIMARY TUMORS AT
SPECIFIC SITES IN FEMALE MICE TREATED WITH 1,5-NAPHTHALENEDIAMINE[a]

TOPOGRAPHY:MORPHOLOGY	CONTROL	LOW DOSE	HIGH DOSE
Lung: Alveolar/Bronchiolar Carcinoma[b]	0/49(0.00)	1/48(0.02)	3/46(0.07)
P Values[c]	N.S.	N.S.	N.S.
Relative Risk (Control)[d]	---	Infinite	Infinite
Lower Limit	---	0.055	0.638
Upper Limit	---	Infinite	Infinite
Weeks to First Observed Tumor	---	89	91
Lung: Alveolar/Bronchiolar Adenoma or Alveolar/Bronchiolar Carcinoma[b]	0/49(0.00)	10/48(0.21)	5/46(0.11)
P Values[c]	N.S.	P = 0.001	P = 0.024
Departure from Linear Trend[e]	P = 0.005	---	---
Relative Risk (Control)[d]	---	Infinite	Infinite
Lower Limit	---	3.037	1.347
Upper Limit	---	Infinite	Infinite
Weeks to First Observed Tumor	---	89	91
Hematopoietic System: Leukemia or Malignant Lymphoma[b]	13/49(0.27)	19/50(0.38)	5/46(0.11)
P Values[c]	N.S.	N.S.	P = 0.045(N)
Departure from Linear Trend[e]	P = 0.011	---	---
Relative Risk (Control)[d]	---	1.432	0.410
Lower Limit	---	0.760	0.124
Upper Limit	---	2.781	1.117
Weeks to First Observed Tumor	57	63	105

TABLE 6 (CONTINUED)

TOPOGRAPHY:MORPHOLOGY	CONTROL	LOW DOSE	HIGH DOSE
Liver: Hepatocellular Carcinoma[b]	1/46(0.02)	25/49(0.51)	16/46(0.35)
P Values[c]	P = 0.001	P < 0.001	P < 0.001
Departure from Linear Trend[e]	P < 0.001	---	---
Relative Risk (Control)[d]	---	23.469	16.000
Lower Limit	---	4.156	2.683
Upper Limit	---	906.346	646.516
Weeks to First Observed Tumor	109	74	99
Liver: Hepatocellular Adenoma or Hepatocellular Carcinoma[b]	1/46(0.02)	28/49(0.57)	27/46(0.59)
P Values[c]	P < 0.001	P < 0.001	P < 0.001
Departure from Linear Trend[e]	P = 0.002	---	---
Relative Risk (Control)[d]	---	26.286	27.000
Lower Limit	---	4.741	4.874
Upper Limit	---	1030.801	1027.943
Weeks to First Observed Tumor	109	74	99
Stomach: Squamous-Cell Papilloma[b]	0/41(0.00)	3/47(0.06)	0/46(0.00)
P Values[c]	N.S.	N.S.	N.S.
Departure from Linear Trend[e]	P = 0.017	---	---
Relative Risk (Control)[d]	---	Infinite	---
Lower Limit	---	0.529	---
Upper Limit	---	Infinite	---
Weeks to First Observed Tumor	---	105	---

TABLE 6 (CONTINUED)

TOPOGRAPHY:MORPHOLOGY	CONTROL	LOW DOSE	HIGH DOSE
Pituitary: Adenoma NOS, Chromophobe Adenoma or Acidophil Adenoma[b]	3/34(0.09)	4/35(0.11)	1/30(0.03)
P Values[c]	N.S.	N.S.	N.S.
Relative Risk (Control)[d]	---	1.295	0.378
Lower Limit	---	0.238	0.007
Upper Limit	---	8.188	4.424
Weeks to First Observed Tumor	109	105	106
Adrenal: Pheochromocytoma[b]	3/46(0.07)	0/44(0.00)	0/44(0.00)
P Values[c]	P = 0.040(N)	N.S.	N.S.
Relative Risk (Control)[d]	---	0.000	0.000
Lower Limit	---	0.000	0.000
Upper Limit	---	1.731	1.731
Weeks to First Observed Tumor	68	---	---
Thyroid: C-Cell Carcinoma[b]	0/44(0.00)	1/49(0.02)	6/45(0.13)
P Values[c]	P = 0.005	N.S.	P = 0.014
Relative Risk (Control)[d]	---	Infinite	Infinite
Lower Limit	---	0.048	1.574
Upper Limit	---	Infinite	Infinite
Weeks to First Observed Tumor	---	105	105

TABLE 6 (CONCLUDED)

TOPOGRAPHY:MORPHOLOGY	CONTROL	LOW DOSE	HIGH DOSE
Thyroid: C-Cell Adenoma or C-Cell Carcinoma[b]	0/44(0.00)	2/49(0.04)	8/45(0.18)
P Values[c]	P = 0.001	N.S.	P = 0.003
Relative Risk (Control)[d]	---	Infinite	Infinite
Lower Limit	---	0.267	2.250
Upper Limit	---	Infinite	Infinite
Weeks to First Observed Tumor	---	105	41
Thyroid: Papillary Adenoma, Follicular-Cell Adenoma, or Papillary Cystadenoma NOS[b]	2/44(0.05)	17/49(0.35)	14/45(0.31)
P Values[c]	P = 0.003	P < 0.001	P = 0.001
Departure from Linear Trend[e]	P = 0.025	---	---
Relative Risk (Control)[d]	---	7.633	6.844
Lower Limit	---	1.971	1.709
Upper Limit	---	64.662	58.827
Weeks to First Observed Tumor	80	105	91

[a]Treated groups received doses of 0.1 or 0.2 percent in feed.

[b]Number of tumor-bearing animals/number of animals examined at site (proportion).

[c]The probability level for the Cochran-Armitage test is given beneath the incidence of tumors in the control group when P < 0.05; otherwise, not significant (N.S.) is indicated. The probability level for the Fisher exact test for the comparison of a treated group with the control group is given beneath the incidence of tumors in the treated group when P < 0.05; otherwise, not significant (N.S.) is indicated. For both Cochran-Armitage and Fisher exact tests a negative designation (N) indicates a lower incidence in the treated group(s) than in the control group.

[d]The 95% confidence interval on the relative risk of the treated group to the control group.

[e]The probability level of the test for departure from linear trend is given beneath the control group when P < 0.05.

not. When incidences were combined so that the numerator represented mice with either a papillary adenoma, a follicular-cell adenoma, or a papillary cystadenoma of the thyroid, the Cochran-Armitage test indicated a significant positive association between dietary concentration and tumor incidence for both males ($P < 0.001$) and females ($P = 0.003$). These were supported by significant ($P \leq 0.006$) Fisher exact test results in each sex for comparisons of each dosed group to the control group. Based on these results, the administration of 1,5-naphthalenediamine was associated with the incidence of thyroid neoplasms in both male and female mice.

For females an increased incidence of hepatocellular carcinomas was also observed among the dosed mice. The Cochran-Armitage test indicated a significant ($P = 0.001$) positive association between dose and incidence. This was supported by significant ($P < 0.001$) comparisons of both the high and low dose to the control group using the Fisher exact test. Based on these results the administration of 1,5-naphthalenediamine was associated with the incidence of hepatocellular carcinomas in female mice.

For female mice, when the incidence of alveolar/bronchiolar adenomas and alveolar/bronchiolar carcinomas were combined, an increased incidence in the dosed groups was noted. The Fisher exact test was significant for both the high ($P = 0.024$) and low ($P = 0.001$) dose groups. The departure from linear trend was significant since tumor incidence was increased more in the low dose than in the high

dose group. In historical control data compiled by this laboratory for the NCI Carcinogenesis Testing Program, 17/275 (6 percent) of the untreated female B6C3F1 mice had an alveolar/bronchiolar neoplasm. Based upon these results the administration of 1,5-naphthalenediamine was associated with the incidence of alveolar/bronchiolar neoplasms in female mice.

For females the Fisher exact test comparing the incidence of leukemia or malignant lymphoma in high dose mice with that in the controls had a probability level in the negative direction of $P = 0.045$, a marginal result which was not significant under the Bonferroni criterion.

Also for females the Cochran-Armitage test showed a significant ($P = 0.040$) negative association between dose and the incidence of adrenal pheochromocytomas, but the Fisher exact tests were not significant.

In male mice the possibility of a negative association between dose and the incidence of malignant lymphomas or leukemia was noted.

Based upon these statistical results the administration of 1,5-naphthalenediamine was associated with the increased incidence of thyroid neoplasms in male mice and of thyroid neoplasms, of hepatocellular carcinomas, and of alveolar/bronchiolar neoplasms in female mice.

V. DISCUSSION

There were no significant positive associations between dietary concentrations of 1,5-naphthalenediamine and mortality in either sex of rats or mice. In all groups adequate numbers of animals survived sufficiently long to be at risk from late-developing tumors.

Several uterine neoplasms occurred in dosed female rats at higher incidences than in corresponding controls. There was a significant positive association between dietary concentration of the compound and the incidences of endometrial stromal polyps in female rats. In addition, the high dose to control Fisher exact comparison was significant. Endometrial stromal sarcomas were observed in two low dose and two high dose female rats, but not in controls. Uterine adenocarcinomas occurred at a higher incidence in the high dose female rat group than in the control group, but the difference in tumor incidence was not statistically significant.

The administration of 1,5-naphthalenediamine was associated with an elevated incidence of clitoral gland neoplasms in female rats. There was a significant positive association between the concentration of the chemical added to the diet and the incidence of either adenomas or carcinomas of the clitoral gland in female rats. The incidence of either of these neoplasms in the high dose female rat group was significant relative to the incidence in the control group.

Elevated incidences of thyroid neoplasms were observed among dosed mice. For mice of both sexes there were significant positive

associations between dietary concentration of 1,5-naphthalenediamine and the incidences of thyroid C-cell carcinomas. For the females the high dose to control Fisher exact comparison supported the finding; this was not true for males. When the mice were grouped so that the numerator of the incidence represented those animals with a papillary adenoma, a follicular-cell adenoma, or a papillary cystadenoma of the thyroid, the Cochran-Armitage test was significantly positive for both males and females and all the Fisher exact comparisons supported the findings.

The incidence of hepatocellular carcinomas in female mice was significantly associated with increased concentration of 1,5-naphthalenediamine. In addition, the high dose to control and the low dose to control Fisher exact comparisons were significant. The incidence of alveolar/bronchiolar adenomas was significant, relative to controls, in both the low dose and the high dose female mouse groups.

Under the conditions of this bioassay, 1,5-naphthalenediamine was carcinogenic in female Fischer 344 rats, causing clitoral and uterine neoplasms. 1,5-Naphthalenediamine was also carcinogenic for B6C3F1 mice, producing thyroid neoplasms in males and neoplasms of the thyroid, liver, and lung in females. Insufficient evidence was provided for the carcinogenicity of the compound in male Fischer 344 rats.

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Review of the Bioassay of 1,5-Naphthalenediamine*
for Carcinogenicity
by the Data Evaluation/Risk Assessment Subgroup
of the Clearinghouse on Environmental Carcinogens

June 29, 1978

The Clearinghouse on Environmental Carcinogens was established in May, 1976, in compliance with DHEW Committee Regulations and the Provisions of the Federal Advisory Committee Act. The purpose of the Clearinghouse is to advise the Director of the National Cancer Institute (NCI) on its bioassay program to identify and to evaluate chemical carcinogens in the environment to which humans may be exposed. The members of the Clearinghouse have been drawn from academia, industry, organized labor, public interest groups, State health officials, and quasi-public health and research organizations. Members have been selected on the basis of their experience in carcinogenesis or related fields and, collectively, provide expertise in chemistry, biochemistry, biostatistics, toxicology, pathology, and epidemiology. Representatives of various Governmental agencies participate as ad hoc members. The Data Evaluation/Risk Assessment Subgroup of the Clearinghouse is charged with the responsibility of providing a peer review of reports prepared on NCI-sponsored bioassays of chemicals studied for carcinogenicity. It is in this context that the below critique is given on the bioassay of 1,5-Naphthalenediamine for carcinogenicity.

The reviewer agreed with the conclusion in the report that 1,5-Naphthalenediamine was carcinogenic in treated female rats and in both sexes of mice. He noted that the study was conducted in a room in which other compounds were under test. Based on the experimental findings, he concluded that 1,5-Naphthalenediamine may pose a carcinogenic risk to humans. The reviewer moved that the report on the bioassay of 1,5-Naphthalenediamine be accepted as written. The motion was approved without objection.

Clearinghouse Members present:

Arnold L. Brown (Chairman), Mayo Clinic
Paul Nettesheim, National Institute of Environmental Health Sciences
Verne Ray, Pfizer Medical Research Laboratory
Verald K. Rowe, Dow Chemical U.S.A.
Michael B. Shimkin, University of California at San Diego
Louise Strong, University of Texas Health Sciences Center

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* Subsequent to this review, changes may have been made in the bioassay report either as a result of the review or other reasons. Thus, certain comments and criticisms reflected in the review may no longer be appropriate.

☆U.S. GOVERNMENT PRINTING OFFICE: 1978-260-899/3198

[redacted]

1. Chemical and Physical Data

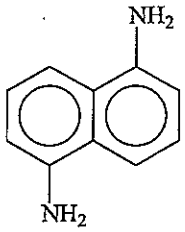
1.1 Synonyms and trade names

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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