N-N-Dimethylaniline; CASRN 121-69-7

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR N-N-Dimethylaniline

File First On-Line 09/30/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/30/1987
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — N-N-Dimethylaniline
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Last Revised — 09/30/1987

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of

information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Splenomegaly, Increased splenic hemosiderosis and hematopoiesis **Mouse Subchronic Gavage Bioassay** **Abdo et al., 1984**	NOEL: None LOAEL: 31.25 mg/kg (converted to 22.32 mg/kg/day)	10,000	1	2E-3 mg/kg/day

*Conversion Factors -- Dose adjusted for gavage schedule (5\days/week).

I.A.2. Principal and Supporting Studies (Oral RfD)

Abdo, K., M. Wolfe and R. Hiles. 1984. Subchronic toxicity of N,N- dimethylaniline to F344 rats and B6C3F1 mice. Fed. Proc. 43(3): 1698.

Groups of F344 rats and B6C3F1 mice (10/sex/species) were treated by gavage with N,N-dimethylaniline in corn oil at 0, 31.25, 62.5, 125, 250, or 500 mg/kg/day, 5 days/week for 13 weeks. There were no effects on mortality. Decreased body weight gain occurred in male rats at greater than or equal to 250 mg/kg/day (or higher), but not in other groups. Clinical signs of toxicity included increased salivation after dosing in all treated groups, a dose-related increased incidence of excessive urination in female rats at greater than or equal to 31.25 mg/kg/day, blanching or cyanosis (or both) in all groups of treated animals at greater than or equal to 125 mg/kg/day, and changes in motor activities at all doses in male mice and at greater than or equal to 125 mg/kg/day in all other groups. Gross and histologic examination revealed a dose-related increased severity of splenomegaly, splenic hemosiderosis, and increased splenic hematopoiesis in all rats at greater than or equal to 31.25 mg/kg/day. Mice had dose-related increases in incidence and severity of splenomegaly at greater than or equal to 31.25 mg/kg/day and in incidence and severity of hemosiderosis and hematopoiesis at greater than or equal to 62.5

mg/kg/day. Hemosiderosis of liver, kidney, and testes was observed at the higher doses (greater than or equal to 125 mg/kg/day). Since adverse effects occurred at the lowest dose tested, a NOAEL or NOEL was not established in this study, and 31.25 mg/kg/day is the LOAEL; by applying an uncertainty factor of 10,000 to this LOAEL, an RfD of 0.002 mg/kg/day was derived.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — An uncertainty factor of 10,000 was applied (10 for interspecies extrapolation, 10 to protect sensitive individuals, 10 because the effect level was a LOAEL and 10 because the study was subchronic.

MF — None

I.A.4. Additional Studies/Comments (Oral RfD)

An abstract of a Russian study (Markosyan, 1969) reported increased muscle chronaxy, increased hemoglobin levels, and an increase in urinary coproporphyrin in rats exposed by inhalation to N,N-dimethylaniline at 0.3 mg/cu.m (converted to an equivalent oral dose of 0.1 mg/kg/day) continuously for 100 days. No effects were observed at 0.04 or 0.005 mg/cu.m (0.01 or 0.002 mg/kg/day). Although this study reports a lower LOAEL and a NOEL, it cannot be used to derive an RfD; it cannot be considered as supportive of the subchronic gavage study because it was reported in limited detail, histopathologic effects were not examined, and many uncertainties are associated with route-to-route extrapolation.

In a reproduction study, no effects on survival or weight gain of dams or birth weight, weight gain, or viability of the offspring through the first 3 postpartum days were observed in mice treated by gavage with N,N- dimethylaniline in corn oil at 365 mg/kg/day on days 7-14 of gestation (Piccirillo et al., 1983). Treatment-related deaths, however, occurred in 3/10 mice treated with the same dose in a range-finding experiment. This study is not adequate for assessment of teratogenic or reproductive toxicity.

ACGIH (1986) adopted a TLV for N,N-dimethylaniline of 5 ppm (25 mg/cu.m) based on its similar toxicity to aniline. Although the TLV of 5 ppm (converted to an equivalent oral dose of 0.6 mg/kg/day) may provide protection, it cannot be used to derive an RfD because it is based on analogy, and uncertainties are associated with route-to-route extrapolation.

I.A.5. Confidence in the Oral RfD

Study — Low
Database — Low
RfD — Low

Confidence in the chosen study is considered low to medium because, although both sexes of two species were studied at several dose levels by a relevant route, the study did not define a NOEL or NOAEL. Confidence in the database is low because supporting oral chronic studies were lacking. The low confidence in RfD reflects the low confidence in the study and database.

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — U.S. EPA, 1986

Limited peer review and extensive agency-wide review, 1986.

Other EPA Documentation — None

Agency Work Group Review — 01/06/1987

Verification Date — 01/06/1987

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for N-N-Dimethylaniline conducted in November 2001 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — N-N-Dimethylaniline
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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — N-N-Dimethylaniline
CASRN — 121-69-7

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — N-N-Dimethylaniline
CASRN — 121-69-7

VI.A. Oral RfD References

Abdo, K., M. Wolfe and R. Hiles. 1984. Subchronic toxicity of N,N-di- methylaniline to F344 rats and B6C3F1 mice. Fed. Proc. 43(3): 1698.

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Documentation of the threshold limit values and biological exposure indices, 5th ed. Cincinnati, OH. p. 207.

Markosyan, T.M. 1969. Comparative toxicity of monomethylaniline and dimethylaniline in chronic experimental exposure. Gig. Sanit. 34(3): 7-11.

Piccirillo, V.J., D.L. McCall, C. Lunchick, L.J. Plankenhom and C. Sexsmith. 1983. Screening of priority chemicals for reproductive hazards. NTIS PB 83- 2576000. p. 108.

U.S. EPA. 1986. Health and Environmental Effect Profile on N,N- Dimethylaniline. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — N-N-Dimethylaniline
CASRN — 121-69-7

Date	Section	Description
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — N-N-Dimethylaniline
CASRN — 121-69-7
Last Revised — 09/30/1987

- 121-69-7
- ANILINE, N,N-DIMETHYL-

- BENZENAMINE, N,N,-DIMETHYL-
- DIMETHLYANILINE
- (DIMETHYLAMINO)BENZENE
- DIMETHYLANILINE
- Dimethylaniline, N-N-
- DIMETHYLPHENYLAMINE
- DWUMETYLOANILINA
- NCI-C56428
- N-N-Dimethylaniline
- N,N-DIMETHYLBENZENEAMINE
- N,N-DIMETHYLPHENYLAMINE
- UN 2253