

## Diphenylamine; CASRN 122-39-4

Health assessment information on a chemical substance is included in IRIS 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 Diphenylamine

**File First On-Line 01/31/1987**

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	01/31/1987
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 — Diphenylamine

CASRN — 122-39-4

Last Revised — 01/31/1987

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
Decreased body weight gain, and increased liver and kidney weights	NOEL: 0.01% of diet (2.5 mg/kg/day)	100	1	2.5E-2 mg/kg/day
2-Year Dog Feeding Study	LEL: 0.1% of diet (25 mg/kg/day)			
Thomas et. al., 1967				

\*Conversion Factors -- 0.01% (1 ppm) = 0.025 mg/kg/day (assumed dog food consumption)

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

Thomas, J.O., W.E. Ribelin, J.R. Woodward and F. Deeds. 1967. The chronic toxicity of diphenylamine for dogs. Toxicol. Appl. Pharmacol. 11: 184-194.

Eight male and 8 female purebred beagles were fed 0.01, 0.1, and 1% diphenylamine in the diet for 2 years. Decreased weight gain and anemia were noted at 0.1 and 1%. At 1%, increases in liver and kidney weights were observed.

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

UF — An uncertainty factor of 100 was used to account for inter- and intra- species differences.

MF — None

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

## Data Considered for Establishing the RfD

- 1) 2-Year Feeding - Dog: Principal study - see discussion above
- 2) 2-Year Feeding (oncogenic) - rat: NOEL=3.1 mg/kg/day; LEL=31 mg/kg/day (kidney lesions) (Chemley Products, 1967)
- 3) 2-Generation Reproduction - rat: Fetotoxic NOEL=125 mg/kg/day; Fetotoxic LEL=250 mg/kg/day (reduced litter size and weight of young) (Food and Agriculture Organization of the United Nations, 1970)

Data Gap(s): Teratology - Rat; Teratology - Rabbit

### **I.A.5. Confidence in the Oral RfD**

Study — Medium  
Database — Medium  
RfD — Medium

The principal study appears to be of good quality and is given a medium confidence rating. Since the database on chronic toxicity is supportive but incomplete, it is given a medium confidence rating. Medium confidence in the RfD follows.

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

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — Pesticide Registration Files

Agency Work Group Review — 07/22/1986

Verification Date — 07/22/1986

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 Diphenylamine conducted in August 2003 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](mailto: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](mailto:hotline.iris@epa.gov) (internet address).

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

Substance Name — Diphenylamine  
CASRN — 122-39-4

Not available at this time.

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## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Diphenylamine  
CASRN — 122-39-4

Not available at this time.

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**III. [reserved]**

**IV. [reserved]**

**V. [reserved]**

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## **VI. Bibliography**

Substance Name — Diphenylamine  
CASRN — 122-39-4

### **VI.A. Oral RfD References**

Chemley Products. 1967. MRID No. 00050962. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Food and Agriculture Organization of the United Nations. 1970. 1969 Evaluations of Some Pesticide Residues in Food. Rome, Italy. p. 91-99.

Thomas, J.O., W.E. Ribelin, J.R. Woodward and F. Deeds. 1967. The chronic toxicity of diphenylamine for dogs. Toxicol. Appl. Pharmacol. 11: 184-194.

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## VI.B. Inhalation RfC References

None

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## VI.C. Carcinogenicity Assessment References

None

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## VII. Revision History

Substance Name — Diphenylamine  
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Date	Section	Description
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.

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## VIII. Synonyms

Substance Name — Diphenylamine  
CASRN — 122-39-4  
Last Revised — 01/31/1987

- 122-39-4
- Aniline, N-phenyl-
- Anilinobenzene
- Benzenamine, N-phenyl-
- Benzene, anilino-

- Benzene, (phenylamino)-
- Big Dipper
- C.I. 10355
- DFA
- Diphenylamine
- DPA
- N,N-Diphenylamine
- No Scald
- N-Phenylaniline
- N-Phenylbenzenamine
- Scaldip