

Diphenamid; CASRN 957-51-7

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 Diphenamid

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 — Diphenamid

CASRN — 957-51-7

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
Liver toxicity	NOEL: 3 mg/kg/day	100	1	3E-2 mg/kg/day
2-Year Dog Feeding Study	LEL: 10 mg/kg/day			
Upjohn Co., 1966a				

*Conversion Factors -- none

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

Upjohn Company. 1966a. MRID No. 00076382. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Groups of purebred beagle dogs, 3 of each sex, were fed 0, 3, 10, or 30 mg/kg/day diphenamid for 2 years. Daily observations were made for the occurrence of untoward clinical signs, changes in food consumption, behavioral changes, stool consistency, urinary excretion, and indications of emesis. Histopathologic observations revealed no distinction between treated and control dogs, with the exception of an increase in portal macrophages and fibroblasts in the 10 and 30 mg/kg/day groups. A slight increase in liver weight occurred in the 10 and 30 mg/kg/day groups. At 30 mg/kg/day these effects were noted in a greater number of dogs.

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

UF — Based on a chronic exposure study, an uncertainty factor of 100 was used to account for the inter- and intraspecies 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 previous description; core grade minimum
- 2) 2-Year Feeding (oncogenic) - rat: Systemic NOEL=10 mg/kg/day; Systemic LEL=30 mg/kg/day (increase of liver (male and female) and thyroid (female) weight); core grade supplementary (Upjohn Co., 1966b)
- 3) 3-Generation Reproduction - rat: Fetotoxic NOEL=10 mg/kg/day; Fetotoxic LEL=30 mg/kg/day (liver congestion, hepatic cell glycogen depletion and irregular hepatic cell size); core grade minimum (Upjohn, 1966c)

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

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — Medium

RfD — Medium

The principal study appears to be of acceptable quality and is given a medium confidence rating. The database on chronic toxicity is incomplete, and is, therefore, given a medium confidence. Medium confidence in the RfD follows.

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

Pesticide Registration Files

Agency Work Group Review — 06/10/1986, 03/18/1987

Verification Date — 03/18/1987

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 Diphenamid conducted in September 2002 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to 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 — Diphenamid
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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Diphenamid
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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 — Diphenamid
CASRN — 957-51-7

VI.A. Oral RfD References

Upjohn Company. 1966a. MRID No. 00076382. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Upjohn Company. 1966b. MRID No. 00076381. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Upjohn Company. 1966c. MRID No. 00076383. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

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

VIII. Synonyms

Substance Name — Diphenamid
CASRN — 957-51-7
Last Revised — 09/30/1987

- 80W
- 957-51-7
- ACETAMIDE, N,N-DIMETHYL-2,2-DIPHENYL-
- BENZENEACETAMIDE, N,N-DIMETHYL-alpha-PHENYL-
- DIAMIDE
- DIF 4
- DIMID
- Diphenamid

- DIPHENAMIDE
- DIPHENYLAMIDE
- 2,2-DIPHENYL-N,N-DIMETHYLACETAMIDE
- DYMID
- ENIDE
- ENIDE 50
- FDN
- FENAM
- L-34314
- N,N-DIMETHYLDIPHENYLACETAMIDE
- N,N-DIMETHYL-2,2-DIPHENYLACETAMIDE
- N,N-DIMETHYL-alpha,alpha-DIPHENYLACETAMIDE
- N,N-DIMETHYL-alpha-PHENYLBENZENEACETAMIDE
- U 4513