Hexazinone; CASRN 51235-04-2

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 Hexazinone

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 — Hexazinone
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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 **2-Year Rat Feeding Study** **du Pont, 1977**	NOEL: 200 ppm diet (10 mg/kg/day) LEL: 1000 ppm diet (50 mg/kg/day)	300	1	3.3E-2 mg/kg/day

*Conversion Factors -- l ppm = 0.05 mg/kg/day (assumed rat food consumption)

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

E.I. du Pont de Nemours & Company. 1977. MRID No. 00078045, 00108638. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Three hundred and sixty Charles River CD rats were divided into five groups of 36 males and females each and fed hexazinone for 2 years at levels of 0 (two groups), 200, 1000, or 2500 ppm. The average body weight gains of males and females receiving 2500 ppm and females receiving l000 ppm were lower than those of the controls and other test groups. There was no clinical, hematologic, or urinary evidence of toxicity.

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

UF — An uncertainty factor of l00 was used to account for inter- and intraspecies differences. An additional UF of 3 was used to account for the lack of a chronic exposure study in an apparently more sensitive species (dogs). A comparison of the 90-day rat and dog studies shows dogs to be more sensitive. Furthermore, a 2-year rat study shows that effects are seen at lower dose levels with chronic exposure; thus, it cannot be predicted that a chronic NOEL in a second mammalian species (for example, dogs) would not affect the RfD.

MF — None

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

Data Considered for Establishing the RfD:

l) 2-Year Feeding (oncogenic) - rat: Principal study - see previous description; core grade minimum

2) 90-Day Feeding - dog: NOEL=25 mg/kg/day; LEL=125 mg/kg/day (decreased body weight, increased SAP and liver weight); core grade minimum (du Pont, 1973)

3) 3-Generation Reproduction - rat: Reproduction NOEL=125 mg/kg/day [HDT]; core grade minimum (du Pont, 1979)

4) Teratology - rat: Maternal NOEL=50 mg/kg/day; Maternal LEL=250 mg/kg/day (decreased food consumption and body weight); Teratogenic NOEL=250 mg/kg/day [HDT]; no core grade (du Pont, 1974)

5) Teratology - rabbit: Teratogenic and Fetotoxic NOEL=125 mg/kg/day [HDT]; LEL=none; core grade minimum (du Pont, 1980)

6) 90-Day Feeding - rat: NOEL=1000 ppm (50 mg/kg/day); LEL=5000 ppm (250 mg/kg/day) no core grade (du Pont, 1973)

Other Data Reviewed:

l) 2-Year Feeding (oncogenicity) - mouse: Systemic NOEL=30 mg/kg/day; Systemic LEL=375 mg/kg/day (liver hypertrophy); core grade minimum (du Pont, 1981)

Data Gap(s): Chronic Dog Feeding Study

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Medium
RfD — Medium

The principal study is of good quality and is given a medium confidence rating. Additional studies are of good quality, but a chronic study in what appears to be a more sensitive

mammalian species (dogs) is lacking; therefore, confidence in the database can be considered medium to high. Confidence in the RfD can also be considered medium to high.

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

Pesticide Registration Standard, l982

Pesticide Registration Files

Agency Work Group Review — 08/05/1986, 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 Hexazinone conducted in September 2002 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 — Hexazinone
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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Hexazinone
CASRN — 51235-04-2

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 — Hexazinone
CASRN — 51235-04-2

VI.A. Oral RfD References

E.I. du Pont de Nemours & Company. 1973. MRID No. 00104977. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

E.I. du Pont de Nemours & Company. 1974. MRID No. 00064258. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

E.I. du Pont de Nemours & Company. 1977. MRID No. 00078045, 00108638. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

E.I. du Pont de Nemours & Company. 1979. MRID No. 00108638. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

E.I. du Pont de Nemours & Company. 1980. MRID No. 00028863. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

E.I. du Pont de Nemours & Company. 1981. MRID No. 00079203, 41359301. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Hexazinone
CASRN — 51235-04-2

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

VIII. Synonyms

Substance Name — Hexazinone
CASRN — 51235-04-2
Last Revised — 09/30/1987

- 51235-04-2
- 3-CYCLOHEXYL-6-(DIMETHYLAMINO)-1-METHYL-1,3,5-TRIAZINE-2,4(1H,3H)-DIONE
- 3-CYCLOHEXYL-6-(DIMETHYLAMINO)-1-METHYL-s-TRIAZINE-2,4(1H,3H)-DIONE
- DPX 3674
- Hexazinone
- s-TRIAZINE-2,4(1H,3H)-DIONE, 3-CYCLOHEXYL-6-(DIMETHYLAMINO)-1-METHYL-
- VELPAR