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Disulfoton (CASRN 298-04-4)

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Reference Dose for Chronic Oral Exposure (RfD)

0154

Disulfoton; CASRN 298-04-4

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Disulfoton

File First On-Line 03/31/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	03/01/1988
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	no data	

_I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Disulfoton

CASRN — 298-04-4

Last Revised — 03/01/1988

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
ChE inhibition, optic nerve degeneration	NOEL: None LEL: 0.8 ppm diet (0.04 mg/kg/day)	1000	1	4E-5 mg/kg/day
2-year Rat Study Oral Exposure (diet)				
Mobay Chemical, 1985				

*Conversion Factors -- 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

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

Mobay Chemical Company. 1985. MRID No. 00129456, 00146873, 41115401. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Disulfoton was fed to male and female Fischer 344 rats at 0.8, 3.3, or 13 ppm in the diet for 105 weeks (the intended concentrations were 1, 4, and 16 ppm). Dose-related inhibition of cholinesterase was observed for plasma, erythrocyte, and brain in both sexes in all treated groups. Histopathologic changes were observed in both sexes. Optic nerve degeneration was observed in a dose-dependent manner in the low-, mid-, and high-dose females, but was statistically significant only at the mid- and high-dose levels.

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

UF — An uncertainty factor of 100 was used to account for the interspecies differences and the spectrum of sensitivity in the human population, plus a 10-fold factor to account for the lack of a no-effect level.

MF — None

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

Data Considered for Establishing the RfD:

- 1) 2-Year Feeding (oncogenic) - rat: Principal study - see previous description; core grade minimum
- 2) 2-Year Feeding - dog: NOEL=1 ppm (0.025 mg/kg/day); LEL=2 ppm (0.05 mg/kg/day) (cholinesterase inhibition); core grade minimum (Mobay Chemical, 1975a)

3) 2-Year Feeding (oncogenic) - rat: RBC ChE and brain ChE: NOEL=1 ppm (0.05 mg/kg/day); LEL=2 ppm (0.1 mg/kg/day); Systemic Toxicity: No NOEL could be determined from available data. (Higher mortality in males at 2 ppm; in males, increase in both absolute and relative weights of spleen, liver, and pituitary, and decrease in both absolute and relative weights of brain and seminal vesicles; in females, decrease in both absolute and relative weight of kidneys); core grade supplementary (incomplete necropsy and histopathology data) (Mobay Chemical, 1975b)

4) Teratology - rat: Teratogenic NOEL=1.0 mg/kg/day (HDT); Fetotoxic NOEL=0.3 mg/kg/day, Fetotoxic LEL=1.0 mg/kg/day (incomplete ossification of the parietals and sternebrae); ChE NOEL=0.1 mg/kg/day; ChE LEL=0.3 mg/kg/day (depressed RBC and plasma ChE activity); Reproduction NOEL=1.0 mg/kg/day (HDT); Maternal NOEL=1.0 mg/kg/day (HDT); core grade minimum (Mobay Chemical, 1983)

5) Teratology - rabbit: Teratogenic NOEL=1.5 mg/kg/day (HDT); Maternal NOEL=1.0 mg/kg/day; Maternal LEL=1.5 mg/kg/day (mortality); core grade minimum (Mobay Chemical, 1982)

6) 3-Generation Reproduction - rat: RBC ChE in F3b litters and their parents LEL=2 ppm (0.1 mg/kg/day); Systemic Toxicity: In F3b litters at 10 ppm (0.5 mg/kg/day) (males and females had cloudy swelling and fatty infiltration in liver; also, females had mild nephropathy in kidney and males had juvenile hypoplasia in testes); Reproductive Effect: No NOEL could be determined from available data. (Reduced fertility and litter size in the first and third generation at 10 ppm dietary level); core grade supplementary (no data on litter weight at birth and their growth rate until weaned. No data on number of stillborn animals; no statistical analysis; incomplete necropsy reports and insufficient histologic data. (Mobay Chemical, 1965)

Data Gap(s): Rat Reproduction Study; Additional studies to evaluate the eye effects (functional impairment of the eye).

___I.A.5. Confidence in the Oral RfD

Study — High
Database — Medium
RfD — Medium

The principal study appears to be of good quality, although a NOEL is lacking for the critical effect; the study is given a high to medium rating. Additional studies appear to be of fair to good quality, and therefore, confidence in the database is considered medium to high. Confidence in the RfD is also considered medium to high.

___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 Standard, April 1984; Pesticide Registration Files

Agency Work Group Review — 05/14/1986

Verification Date — 05/14/1986

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 Disulfoton 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 — Disulfoton
CASRN — 298-04-4

Not available at this time.

__II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Disulfoton
CASRN — 298-04-4

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 — Disulfoton
CASRN — 298-04-4
Last Revised — 02/01/1990

__VI.A. Oral RfD References

Mobay Chemical Company. 1965. MRID No. 00057267, 00091104. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Company. 1975a. MRID No. 00073348. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Company. 1975b. MRID No. 00069966, 00154957. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Company. 1982. MRID No. 00147886. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Company. 1983. MRID No. 00129458. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Company. 1985. MRID No. 00129456, 00146873, 41115401. 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 — Disulfoton
CASRN — 298-04-4

Date	Section	Description
03/01/1988	I.A.5.	Confidence levels revised
02/01/1990	VI.	Bibliography on-line
01/01/1992	IV.	Regulatory actions updated
04/01/1997	III., IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

_VIII. Synonyms

Substance Name — Disulfoton
CASRN — 298-04-4
Last Revised — 03/31/1987

298-04-4
BAY 19639
BAYER 19639
DIMAZ
DISULFATON
Disulfoton

DI-SYSTON
 DISYSTOX
 DITHIODEMETON
 DITHIOPHOSPHATE DE O,O-DIETHYLE ET DE S-(2-ETHYLTHIO-ETHYLE)
 DITHIOSYSTOX
 ENT 23,437
 FRUMIN AL
 FRUMIN G
 M-74
 NA 2783
 O,O-DIAETHYL-S-(2-AETHYLTHIO-AETHYL)-DITHIOPHOSPHAT
 O,O-DIAETHYL-S-(3-THIA-PENTYL)-DITHIOPHOSPHAT
 O,O-DIETHYL 2-ETHYLTHIOETHYL PHOSPHORODITHIOATE
 O,O-DIETHYL S-(2-ETHTHIOETHYL) PHOSPHORODITHIOATE
 O,O-DIETHYL S-(2-ETHTHIOETHYL) THIOTHIONOPHOSPHATE
 O,O-DIETHYL S-(2-ETHYLMERCAPTOETHYL) DITHIOPHOSPHATE
 O,O-DIETHYL-S-(2-ETHYLTHIO-ETHYL)-DITHIOFOSFAAT
 O,O-DIETHYL S-2-(ETHYLTHIO)ETHYL PHOSPHORODITHIOATE
 O,O-DIETHYL-S-(2-ETILTIO-ETIL)-DITIOFOSFATO
 O,O-ETHYL S-2(ETHYLTHIO)ETHYL PHOSPHORODITHIOATE
 PHOSPHORODITHIOIC ACID, O,O-DIETHYL S-(2-(ETHYLTHIO)ETHYL) ESTER
 PHOSPHORODITHIONIC ACID, S-2-(ETHYLTHIO)ETHYL-O,O-DIETHYL ESTER
 RCRA WASTE NUMBER P039
 S 276
 S-2-(ETHYLTHIO)ETHYL O,O-DIETHYL ESTER of PHOSPHORODITHIOIC ACID
 SOLVIREX
 THIODEMETON
 THIODEMETRON

<http://www.epa.gov/iris/subst/0154.htm>
 Last updated on Monday, March 07, 2011

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Uncertainty and
Modifying Factors
Additional
Studies/Comments
Confidence in the
Inhalation RfC
EPA
Documentation
and Review

**Carcinogenicity
Assessment for
Lifetime Exposure**

**Evidence for Human
Carcinogenicity**

Weight-of-
Evidence
Characterization
Human
Carcinogenicity
Data
Animal
Carcinogenicity
Data
Supporting Data
for
Carcinogenicity

**Quantitative
Estimate of
Carcinogenic Risk
from Oral Exposure**

Summary of Risk
Estimates
Dose-Response
Data
Additional
Comments
Discussion of
Confidence

**Quantitative
Estimate of
Carcinogenic Risk
from Inhalation
Exposure**

Summary of Risk
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Additional
Comments
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EPA
Documentation,
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Bibliography

Revision History

Synonyms