

Rotenone; CASRN 83-79-4

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 Rotenone

File First On-Line 09/07/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/07/1988
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 — Rotenone

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Last Revised — 09/07/1988

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
Reduced pup weight	NOEL: 7.5 ppm (0.38 mg/kg/day)	100	1	4E-3 mg/kg/day
2-Generation Rat Reproduction Study	LEL: 37.5 ppm (1.88 mg/kg/day)			
U.S. Fish and Wildlife Service, 1983				

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

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

U. S. Fish and Wildlife Service. 1983. MRID No. 00141408 Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Diets containing 0, 7.5, 37.5, or 75 ppm (0, 0.38, 1.88, or 3.8 mg/kg/day) rotenone were given to groups of 15 male and 25 male Charles River CD (SD) BR strain rats through two generations. The first parental generation (F0) animals were 6 weeks old at the beginning of the test, and they were given test diets for 105 days prior to mating. Parental rats were selected from pups 21 days after birth for the second (F1) generation mating, and they were given test diets for a period of 120 days before they were mated. Test diets were also administered during gestation and lactation for both generations. Litter sizes were reduced in the 75 ppm (3.8 mg/kg/day) dose group (highest dose tested) in the F0 and F1a generations indicating a reproductive effect at 75 ppm. Pup weights were reduced in both generations during lactation for the 37.5 and 75 ppm dose groups. Body weights and body weight gains in adult rats were reduced during the two generations also. Based on these results, the lowest effect level for reproductive toxicity (LEL) is 37.5 ppm (1.88 mg/kg/day) and the no-observed effects level (NOEL) is 7.5 ppm (0.38 mg/kg/day).

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

UF — 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-Generation Reproduction - rat: Principal study - see previous description; core grade minimum
- 2) 6-Month Feeding - dog: NOEL=0.4 mg/kg/day; LEL=2 mg/kg/day (decreased mean body weights; decreased hematocrit and hemoglobin; decreased cholesterol, total lipids, and glucose levels in the blood; increased incidence of emesis and diarrhea); core grade guideline (U.S. Fish and Wildlife Service, 1980)
- 3) 2-Year Feeding (oncogenic) - rat: NOEL could not be established because microscopic examination of mid (37.5) and low (7.5 ppm) group animals was not performed; Effects observed at 75 ppm (3.8 mg/kg/day) (HDT) included reduced body weight in males and females, reduced food consumption in females, lower total protein and albumin levels in the blood, increased blood urea nitrogen levels, and increased incidences of adrenal gland angiectasis and hemorrhage; core grade supplementary (U.S. Fish and Wildlife Service, 1985)
- 4) Teratology - mouse: Maternal, Teratogenic, and Fetotoxic NOEL=15 mg/kg/day; LEL=none; core grade minimum when considered with range finding study (U.S. Fish and Wildlife Service, 1981a)
- 5) Teratology (range finding) - mouse: Maternal NOEL=12 mg/kg/day; Maternal LOEL=24 mg/kg/day (HDT; decreased gravid uterine weight and mortality); Fetotoxic NOEL=12 mg/kg/day; Fetotoxic LEL=24 mg/kg/day (HDT; decreased litter size and increased resorptions); core grade supplementary but used to support the main mouse teratology study (U.S. Fish and Wildlife Service, 1981b)
- 6) Teratology - rat: Maternal NOEL=3 mg/kg/day; Maternal LOEL=6 mg/kg/day (decreased body weight); Fetotoxic NOEL=3 mg/kg/day; Fetotoxic LOEL=6 mg/kg/day (increased incidence of unossified sternebrae, renal pelvic cavitation, and distended ureters); core grade minimum (U.S. Fish and Wildlife Service, 1982)

Other Data Reviewed:

1) 2-Year Oncogenic - mouse: No toxicologically significant effects were noted at 1200 ppm (180 mg/kg/day) (HDT); core grade supplementary (NTP, 1986)

Data Gap(s): Chronic Rat Feeding Study

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — Medium

RfD — Medium

The critical study is of adequate quality and is given a medium confidence rating. Since an adequate chronic rodent study is lacking, the database 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 Standard, December 1987; Pesticide Registration Files

Agency Work Group Review — 01/21/1988

Verification Date — 01/21/1988

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 Rotenone 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 — Rotenone
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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Rotenone
CASRN — 83-79-4

Not available at this time.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Rotenone
CASRN — 83-79-4

VI.A. Oral RfD References

NTP (National Toxicology Program). 1986. MRID No. 40179801. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

U.S. Fish and Wildlife Service. 1980. MRID No. 00141406. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

U.S. Fish and Wildlife Service. 1981a. MRID No. 00141407. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

U.S. Fish and Wildlife Service. 1981b. MRID No. 00103047. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

U.S. Fish and Wildlife Service. 1982. MRID No. 00144294. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

U.S. Fish and Wildlife Service. 1983. MRID No. 00141408. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

U.S. Fish and Wildlife Service. 1985. MRID No. 00156739. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Rotenone
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Date	Section	Description
09/07/1988	I.A.	Oral RfD summary on-line
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Rotenone

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Last Revised — 09/07/1988

- 83-79-4
- cube
- derrin
- derris
- derrisroot
- nicouline
- Rotenone
- rotessenol
- tubatoxin