

Difenzoquat; CASRN 43222-48-6

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 Difenzoquat

File First On-Line 08/22/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	08/22/1988
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 — Difenzoquat
CASRN — 43222-48-6
Primary Synonym — Avenge
Last Revised — 08/22/1988

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
Decreased body weight	NOEL: 500 ppm (25 mg/kg/day)	300	1	8E-2 mg/kg/day
2-Year Rat Feeding Study	LEL: 2500 ppm (125 mg/kg/day)			
American Cyanamid Co., 1975				

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

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

American Cyanamid Company. 1975. MRID No. 00037923. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Sixty young Wistar rats of each sex were used per dosage level of 100, 500, and 2500 ppm (5, 25, and 125 mg/kg/day). The 2500 ppm level was changed to 5000 ppm (250 mg/kg/day) after the 30th week. At the 2500/5000 ppm level body weight gain was depressed for both sexes at the 52, 78, and 104 week periods. The NOEL was established at the 500 ppm for this study because of the depressed body weight gain at the high dose level. This effect was not considered to be of a severe nature but rather a consistent one during a significant part of the study.

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

UF — An uncertainty factor of 100 was used, 10 each to account for the inter- and intraspecies differences. An additional UF of 3 was used to account for the lack of a chronic dog study.

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; no core grade
- 2) 90-Day Feeding - dog: Systemic NOEL=2500 ppm (62.5 mg/kg/day) (HDT); no core grade (American Cyanamid Company, 1973)
- 3) 3-Generation Reproduction - rat: Systemic and Reproductive NOEL=2500 ppm (125 mg/kg/day) (HDT); Fetotoxic NOEL=500 ppm (25 mg/kg/day); Fetotoxic LEL=2500 ppm (125 mg/kg/day) (HDT; decreased pups weights at birth and weanling); no core grade (American Cyanamid Company, 1974a)
- 4) Teratology - rat: Systemic, Reproductive, and Teratogenic NOEL=2500 ppm (125 mg/kg/day) (HDT); Systemic, Reproductive, and Teratogenic NOEL=none; no core grade (American Cyanamid Company, 1974)

Other Data Reviewed:

- 1) 18-Month Oncogenic - mice: Systemic NOEL=2500 ppm (375 mg/kg/day) (HDT); no core grade (American Cyanamid Company, 1975b)

Data Gap(s): Chronic Dog Feeding Study; Rabbit Teratology Study

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — Medium

RfD — Medium

The critical study is of fair quality and is given a medium to low confidence rating. A comparison of the 90-day interim sacrifice of the critical study and the 90-day dog study indicates that the dog is probably the most sensitive species; therefore, a chronic dog feeding study is necessary to fully assess the toxicity of difenzoquat. Since a chronic dog 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 Files

Agency Work Group Review — 10/14/1987

Verification Date — 10/14/1987

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 Difenzoquat 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 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 — Difenzoquat

CASRN — 43222-48-6

Primary Synonym — Avenge

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Difenzoquat

CASRN — 43222-48-6

Primary Synonym — Avenge

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 — Difenzoquat

CASRN — 43222-48-6

Primary Synonym — Avenge

VI.A. Oral RfD References

American Cyanamid Company. 1973. MRID No. 00037922. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1974a. MRID No. 00030578. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1974b. MRID No. 00030576. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1975a. MRID No. 00037923. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1975b. MRID No. 00036710. 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 — Difenzoquat

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Primary Synonym — Avenge

Date	Section	Description
08/22/1988	I.A.	Oral RfD summary on-line
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Difenzoquat

CASRN — 43222-48-6

Primary Synonym — Avenge

Last Revised — 08/22/1988

- 43222-48-6
- AC 84777
- Avenge
- Difenzoquat
- difenzoquat methyl sulfate
- 1,2-dimethyl-3,5-diphenyl-1-H-pyrazolium methyl sulfate
- finaven
- mataven
- 1H-pyrazolium, (1,2-dimethyl-3,5-diphenyl)-, methyl sulfate
- yeh-yan-ku