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Dimethoate; CASRN 60-51-5

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 <u>IRIS assessment</u> <u>development process</u>. 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 <u>guidance documents located</u> <u>on the IRIS website</u>.

STATUS OF DATA FOR Dimethoate

File First On-Line 01/31/1987

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	s for Noncarcinogenic Eff	fects
I.A. Reference Dose for Chronic Oral Exposu	re (RfD)	

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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
Brain ChE inhibition	NOEL: 1 ppm diet (0.05 mg/kg/day)	300	1	2E-4 mg/kg/day
2-Year Rat Feeding				
Study	LEL: 5 ppm diet (0.25 mg/kg/day)			
American Cyanamid				
Co., 1986a				

*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. 1986a. MRID No. 00164177, 40545501. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Groups of Wistar SPF rats, 50 males and 50 females/group, were fed 0, 1, 5, 25, and 100 ppm (0, 0.05, 0.25, 1.25, and 5.0 mg/kg/day) of dimethoate in their diets for 2 years. A 2-year satellite study (animals were used for clinical chemistry, hematology, and urinalysis), with 15 rats/sex/dose group was also conducted using the same dose levels. There was a dose dependent lowering of cholinesterase activity in the brain in both males and females receiving 5, 25, and 100 ppm. Plasma and RBC cholinesterase activity was also inhibited in males and females receiving 100 ppm, and growth was retarded in 100 ppm males during the first half of the study. In rats receiving 100 ppm there was a slight anemia which was predominant in males and an increase in leukocytes in both sexes during the second half of the study.

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. An additional UF of 3 was used to account for the lack of a complete database.

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 guideline

2) Cholinesterase - human: NOEL=0.2 mg/kg/day; LEL=0.4 mg/kg/day (plasma and RBC ChE inhibition); no core grade [Fisons (Canada), Ltd., 1958)

3) 90-Day Feeding - dog: ChE NOEL=2 ppm (0.05 mg/kg/day); ChE LEL=10 ppm (0.25 mg/kg/day) (RBC ChE depression); core grade minimum (American Cyanamid Co., 1968)

4) 3-Generation Reproduction - mouse: Reproductive NOEL=50 ppm (7.5 mg/kg/day) (HDT); core grade minimum (American Cyanamid Co., 1965)

5) Teratology - rat: Maternal NOEL=6 mg/kg/day; Maternal LEL=18 mg/kg/day (hypersensitivity, tremors, and unsteady gait); core grade minimum (Khera et al., 1979)

6) Teratology - rabbit: Maternal NOEL=10 mg/kg/day; Maternal LEL=20 mg/kg/day (decreased body weight); core grade supplementary (American Cyanamid, Co., 1984

Other Data Reviewed:

1) 78-Week Feeding (oncogenic) - mouse: Systemic NOEL=none; LEL=25 ppm (3.75 mg/kg/day) (hepatocyte vacuolization in females); ChE NOEL=none; LEL=25 ppm (3.75 mg/kg/day) (RBC and plasma depressed); at 200 ppm (30 mg/kg/day) (HDT) (liver tumors in females and lung and hemolymphorecticular system tumors in males were observed); core grade minimum (American Cyanamid Co., 1986b)

2) 2-Year Feeding (oncogenic) - rat: NOEL=1 ppm (0.05 mg/kg/day); LEL=10 ppm (0.5 mg/kg/day) (plasma and brain ChE inhibition); core grade supplementary (lack of detailed data disallows for histopathological effect) (American Cyanamid Co., 1970)

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

I.A.5. Confidence in the Oral RfD

Study — High Database — Medium RfD — Medium

The critical study is of good quality and is given a high confidence rating. Since a chronic feeding study in a second species 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

Registration Standard, 1982

Registration Files

Agency Work Group Review — 07/08/1985, 07/22/1985, 09/29/1986, 03/18/1987, 03/23/1988

Verification Date — 03/23/1988

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 Dimethoate conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at <u>hotline.iris@epa.gov</u> 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 <u>hotline.iris@epa.gov</u> (internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Dimethoate CASRN — 60-51-5

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Dimethoate CASRN — 60-51-5

Not available at this time.

III. [reserved] IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Dimethoate CASRN — 60-51-5

VI.A. Oral RfD References

American Cyanamid Company. 1965. MRID No. 00045816. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1984. MRID No. 00149126. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1968. MRID No. 00075532. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1986a. MRID No. 00164177, 40545501. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1986b. MRID No. 00163800. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1970. MRID No. 00063995. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Fisons (Canada) Ltd. 1958. MRID No. 00055394. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Khera, K.S., C. Whalen, G. Trivett and G. Angers. 1979. Teratogenicity studies on pesticidal formulations of dimethoate, diuron and lindane in rats. Bull. Environ. Contam. Toxicol. 22(4-5): 522-529.

VI.B. Inhala	ation RfC	References		
None	Y			
VI.C. Carci	nogenicity	Assessment References		
None				
VII. Revision History				
Substance N	ame — Di	methoate		
CASRN — 60-51-5				
Date	Section	Description		
06/30/1988	I.A.	RfD withdrawn		
08/22/1988	I.A.	Revised oral RfD summary added		
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.		

VIII. Synonyms

Substance Name — Dimethoate CASRN — 60-51-5 Last Revised — 01/31/1987

- 60-51-5
- 8014 Bis HC
- Acetic Acid, O,O-Dimethyldithiophosphoryl-, N-Mono-methylamide Salt
- American Cyanamid 12,880
- BI 58
- CL 12880
- Cygon
- Cygon 4E
- Cygon Insecticide
- Daphene
- De-Fend
- Demos-L40
- Dimethoate
- Dimethogen
- Dimeton
- Dimevur
- ENT 24650
- FIP
- Fosfoto R 35
- Fosfotox
- Fosfotox R
- Fostion MM
- Lurgo
- NCI-C00135
- O,O-Dimethyl S-(N-Methyl- carbamoylmethyl Dithiophosphate
- O,O-Dimethyl S-(N-Methylcarbamoylmethyl) Phosphorodithioate
- PEI 75
- Perfecthion
- Perfekthion
- Phosphamid
- Phosphamide
- Phosphor-odithioic Acid, O,O-Dimethyl S-(2-(Methylamino)-2-Oxoethyl) Ester
- Racusan
- Rogor
- Rogor 20L
- Rogor 40
- Rogor L

- Rogor P
- Roxion
- Sinoratox
- S-Methylcarbamoylmethyl O,O-Dimethyl Phosphorodithioate
- Systoate