Demeton; CASRN 8065-48-3

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 Demeton

File First On-Line 01/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	01/31/1987
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 — Demeton
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Last Revised — 01/31/1987

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 **2-Year Feeding in Rats. (Disulfoton)** **Mobay Chemical, 1985**	NOEL: none LEL: 0.8 ppm diet (0.04 mg/kg/day)	1000	1	4E-5 mg/kg/day

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

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

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

Demeton is a mixture of thiol and thiono isomers. The thiol isomer is the same as the oxon metabolite of disulfoton, and the thiono isomer is structurally similar to disulfoton. On this basis, the chronic data submitted for disulfoton were accepted to fulfill requirements for demeton. Since the disulfoton chronic rat study yields the most sensitive endpoint, this study was used for the RfD calculation.

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 (ChE) 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 in 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 inter- and intra- species differences in sensitivity to possible optic nerve degeneration. An additional factor of 10 was applied because a NOEL was not established. Based on the 1984 Demeton Registration Standard, the data requirements for chronic testing of Demeton per se were waived, and the chronic data from disulfoton were used as a surrogate.

MF — None

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

Data Considered for Establishing the RfD

1) 2-Year Feeding (disulfoton) - rat: Principal study - see description above; core grade minimum

2) 2-Year Feeding (disulfoton) - dog: ChE NOEL=1 ppm (0.025 mg/kg/day), ChE LEL=2 ppm (0.05 mg/kg/day); NOEL (other effects)=2 ppm (HDT); core grade minimum (Mobay Chemical, 1975a)

3) 2-Year Feeding (disulfoton) - rat: ChE NOEL=1 ppm (0.05 mg/kg/day), ChE LEL=2 ppm (0.1 mg/kg/day) (RBC and brain ChE inhibition); NOEL (other systemic effects)=none; LEL=2 ppm (males -- higher mortality, 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; females -- decrease in both absolute and relative weight of kidneys); core grade supplementary (Incomplete necropsy and histopathology data) (Mobay Chemical, 1975b)

4) 24-Week Feeding (demeton) - dogs: NOEL=1 ppm (0.025 mg/kg/day); LEL=2 ppm (0.05 mg/kg/day) (inhibition of plasma ChE at 2 ppm, erythrocyte ChE at 5 ppm); core grade supplementary (Ciba-Geigy, 1957)

5) 77 to 112 Day Feeding (demeton) - female rats: ChE NOEL=1 ppm; LEL=3 ppm NOEL (other systemic effects)=10 ppm; LEL=20 ppm (alteration in food intake/body weight ratio); core grade supplementary (Pensalt Chemicals, 1954)

6) 90-Day Feeding Study (demeton)- rats: Systemic NOEL=0.66 mg/kg/day; LEL=0.9 mg/kg/day (tremors and hyperexcitability) (Mobay Chemical, 1955a)

7) 106-Day Feeding (demeton) - rabbits: ChE NOEL=0.15 mg/kg/day; ChE LEL=0.5 mg/kg/day; core grade supplementary (Mobay Chemical, 1955b)

8) Teratology (demeton) - mouse: Developmental NOEL=7 mg/kg/day (i.p. injection); LEL=10 mg/kg/day (i.p.) (possible increase in abnormalities of digestive tract, cleft palate); published report; core grade supplementary (Budreau and Singh, 1973)

Other Data Reviewed:

1) 16-Week Feeding (demeton) - dogs: ChE NOEL=0.75 ppm (0.19 mg/kg/day); LEL=2 ppm (0.05 mg/kg/day); no core grade (Mobay Chemical, 1959)

Data Gaps (demeton): Teratology - rat; Teratology - rabbit; Subchronic feeding - rat; Subchronic feeding- dog; Subchronic feeding on thiolphosphate sulfoxide (plant metabolite)

I.A.5. Confidence in the Oral RfD

Study — High
Database — Low
RfD — Low

The principal study is of good quality, and is given a high rating. However, the database for demeton is incomplete; therefore, confidence in the data base can be considered low to medium. Confidence in the RfD can also be considered low to medium.

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, November 1984; Registration Files.

Agency Work Group Review — 07/22/1986

Verification Date — 07/22/1986

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 Demeton conducted in November 2001 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to 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 — Demeton
CASRN — 8065-48-3

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Demeton
CASRN — 8065-48-3

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 — Demeton
CASRN — 8065-48-3

VI.A. Oral RfD References

Budreau, C.H. and R.P. Singh. 1973. Teratogenicity and embryotoxicity of demeton and fenthion in CF1 mouse embryos. Toxicol. Appl. Pharmacol. 24(2): 324-332.

Ciba-Geigy Corporation. 1957. MRID No. 00061985. Available from EPA. Write to FOI, EPA, Washington DC 20460.

Mobay Chemical Corporation. 1955a. MRID No. 00100906. Available from EPA. Write to FOI, EPA, Washington DC 20460.

Mobay Chemical Corporation. 1955b. MRID No. 00100906. Available from EPA. Write to FOI, EPA, Washington DC 20460.

Mobay Chemical Corporation. 1959. MRID No. 00100908. Available from EPA. Write to FOI, EPA, Washington DC 20460.

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

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

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

Pennsalt Chemicals Corporation. 1954. MRID No. 00087465. 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 — Demeton
CASRN — 8065-48-3

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

VIII. Synonyms

Substance Name — Demeton
CASRN — 8065-48-3
Last Revised — 01/31/1987

- 8065-48-3
- BAY 10756
- BAYER 8169
- Demeton
- DEMETON-O + DEMETON-S
- DEMOX
- DIETHOXY THIOPHOSPHORIC ACID ESTER of 2-ETHYLMERCAPTOETHANOL
- E 1059
- ENT 17,295
- MERCAPTOPHOS
- O,O-DIETHYL 2-ETHYLMERCAPTOETHYL THIOPHOSPHATE
- O,O-DIETHYL O(and S)-2-(ETHYLTHIO)ETHYL PHOSPHOROTHIOATE MIXTURE
- SYSTEMOX
- SYSTOX
- ULV