

Ethion; CASRN 563-12-2

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 Ethion

File First On-Line 03/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/01/1989
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 — Ethion

CASRN — 563-12-2

Last Revised — 09/01/1989

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
Plasma cholinesterase inhibition	NOEL: 0.05 mg/kg/day LEL: 0.075 mg/kg/day	100	1	5E-4 mg/kg/day
Cholinesterase Inhibition Study in Humans				
FMC Corp., 1970				
Inhibition of brain cholinesterase	NOEL: 2.5 ppm (0.06 mg/kg/day)			
90-Day Dog Study Oral Exposure (diet)	LEL: 25 ppm (0.71 mg/kg/day)			
FMC Corp., 1988				

*Conversion Factors -- Actual dose tested

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

FMC Corporation. 1970. MRID No. 00073157. FMC Corporation. 1988. MRID No. 40773301. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

A total of 10 male adult human volunteers ranging in age from 22 to 43 years and in weight from 60.4 to 118.6 kg were used in this study (FMC Corp, 1970). The volunteers were randomly divided into a control group consisting initially of four subjects and a test group consisting of six subjects. Baseline plasma and erythrocyte cholinesterase activities were determined five times

during a 2-week pretreatment period. The test period was divided into four sequential dosing regimens and a recovery period as follows: 1) 0.05 mg/kg/day - 21 days; 2) 0.075 mg/kg/day - 21 days; 3) 0.10 mg/kg/day - 21 days; 4) 0.15 mg/kg/day - 3 days; and 4) Recovery - 19 days. Test material was administered in corn oil solutions at dosages. Dosages were adjusted to body weight on a weekly basis. Control subjects received capsules containing corn oil. During the course of the study, the number of subjects was reduced (1 control subject and 1 test subject).

No consistent effects on plasma or erythrocyte cholinesterase activity were observed at the 0.05 mg/kg/day dose level, the lowest dose tested. Significant reductions of plasma cholinesterase activity from pretreatment levels were observed on day 1 of the 0.075 mg/kg/day dosing regimen and throughout the course of the serially increased dosing (0.10 and 0.15 mg/kg/day) until day 7 of the recovery period. Plasma cholinesterase activity during the 0.075, 0.10, and 0.15 mg/kg/day dosing regimens was reduced to approximately 85, 76, and 69%, respectively, of the pretreatment group mean. On day 7 of the recovery period, plasma activity was 82% of the pretreatment level; activities at days 12 and 19 of the recovery period were not significantly different from pretest levels. At the dose regimen used, erythrocyte cholinesterase activity was not affected by the test material nor was there any effect seen in any of the hematologic parameters measured during the study. Therefore, based on the plasma cholinesterase inhibition observed at 0.075 mg/kg/day, the NOEL for this study is 0.05 mg/kg/day.

Groups of beagle dogs (4/sex/dose) received ethion orally at dietary concentrations of 0, 0.5, 2.5, 25.0, and 300 ppm for 90 days (FMC Corp., 1988). The average compound intake for various groups were 0.01, 0.06, 0.71, and 6.9 mg/kg/day for males and 0.012, 0.07, 0.71, and 8.25 mg/kg/day for females.

Animals receiving 300 ppm showed signs of ataxia, emesis, miosis, and tremors. Male and female dogs of the 300 ppm group also showed a decrease in body weight and food consumption relative to the controls. Clinical chemistry indicated that ethion significantly inhibited brain and erythrocyte cholinesterase activity in males and females receiving 25 and 300 ppm. Thus, the NOEL for these endpoints is 2.5 ppm (0.06 or 0.07 mg/kg/day for males and females, respectively); the LEL=25 ppm. Plasma cholinesterase activity was inhibited in males and females receiving 2.5, 25, and 300 ppm. The decrease in plasma cholinesterase activity was dose-related. No compound-related histomorphologic changes were found in the ethion treated animals. The LEL for plasma cholinesterase activity is 2.5 ppm (0.06 mg/kg/day males; 0.07 mg/kg/day females); the NOEL is 0.5 ppm (0.01 mg/kg/day males; 0.012 mg/kg/day females).

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

UF — An uncertainty factor of 10 was used to account for the differences in sensitivity within the human population. An additional UF of 10 was used to account for the brain cholinesterase inhibition observed at 25 ppm (0.71 mg/kg/day) in the subchronic dog study. An additional UF of 10 for subchronic to chronic extrapolation in the dog study was not used since there is no change in the endpoint over time.

MF — None

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

Data Considered for Establishing the RfD

- 1) Cholinesterase Inhibition - human: Principal study - see previous description; core grade supplementary
- 2) 90-Day Feeding - dog: Principal study - see previous description; core grade minimum
- 3) 2-Year Feeding (oncogenic) - rat: Systemic NOEL=4 ppm (0.2 mg/kg/day); Systemic LEL=40 ppm (2 mg/kg/day) (HDT; depressed plasma ChE); core grade minimum (FMC Corp., 1985a)
- 4) 3-Generation Reproduction - rat: NOEL=4 ppm (0.2 mg/kg/day); LEL=25 ppm (1.25 mg/kg/day) (HDT; significant plasma ChE inhibition in females); Reproductive NOEL=25 ppm (1.25 mg/kg/day) (HDT); Reproductive LEL=none; core grade minimum (FMC Corp., 1985b)
- 5) Teratology - rat: Developmental NOEL=0.6 mg/kg/day; Developmental LEL=2.5 mg/kg/day (sites of delayed ossification of pubes); Maternal NOEL=0.6 mg/kg/day; Maternal LEL=2.5 mg/kg/day (increased incidence of hyperactivity); core grade minimum (FMC Corp., 1983a)
- 6) Teratology - rabbit: Maternal NOEL=0.6 mg/kg/day; Maternal LEL=2.4 mg/kg/day (increased incidence of orange-colored urine and reduced body weight gain in females); Developmental NOEL=2.4 mg/kg/day; Developmental LEL=9.6 mg/kg/day (HDT; increased incidence of fused sternal centers); core grade minimum (FMC Corp., 1983b)

Other Data Reviewed:

- 1) Chronic Feeding (oncogenic) - mouse: NOEL=1.5 ppm (0.225 mg/kg/day); LEL=8 ppm (1.2 mg/kg/day) (HDT; plasma ChE inhibition); core grade minimum (FMC Corp., 1985c)

2) 2-Year Feeding - dog: Plasma ChE NOEL=6 ppm (0.15 mg/kg/day); Plasma ChE LEL=20 ppm (0.5 mg/kg/day) (depression of plasma ChE in females); Chronic NOEL not established due to study deficiencies; control hematology, serum chemistry and urinalysis data missing; core grade supplementary (FMC Corp., 1972)

3) 90-Day Feeding - rat: ChE NOEL=3 ppm (0.15 mg/kg/day); ChE LEL=10 ppm (0.5 mg/kg/day) (decreased plasma ChE activity); Brain and red blood cell cholinesterase activity was reduced at 30 and 100 ppm (1.5 and 5 mg/kg/day); core grade supplementary (FMC Corp., 1958a)

4) 90-Day Feeding - dog: ChE NOEL=1 ppm (0.025 mg/kg/day); ChE LEL=3 ppm (0.75 mg/kg/day) (reduced plasma ChE activity); no core grade (FMC Corp., 1958b)

5) Acute Delayed Neurotoxicity - hen: Acute oral LD50 is 2792 mg/kg/day and did not produce clinical or histopathological signs of neurotoxicity; core grade minimum (FMC Corp., 1986)

Data Gap(s): Chronic Dog 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 the 2-year dog study does not satisfy the data requirement for a chronic oral toxicity study in a non-rodent species, 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

Pesticide Registration Standard, February 1989

Pesticide Registration File

Agency Work Group Review — 09/16/1986, 05/17/1989

Verification Date — 05/17/1989

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 — Ethion
CASRN — 563-12-2

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ethion
CASRN — 563-12-2

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 — Ethion
CASRN — 563-12-2

VI.A. Oral RfD References

FMC Corporation. 1970. MRID No. 00073157. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1988. MRID No. 40773301. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1985a. MRID No. 00148991. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1985b. MRID No. 00148990. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1983a. MRID No. 00131852. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1983b. MRID No. 00131853. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1985c. MRID No. 00148989. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1972. MRID No. 00141845. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1958a. MRID No. 00073077. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1958b. MRID No. 00073708. Available from EPA. Write to FOI, EPA, Washington DC 20460.

FMC Corporation. 1986. MRID No. 00158376. 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 — Ethion
CASRN — 563-12-2

Date	Section	Description
06/01/1989	I.A.	Withdrawn; new Oral RfD verified (in preparation)
09/01/1989	I.A.	Oral RfD summary on-line; RfD changed

VIII. Synonyms

Substance Name — Ethion
CASRN — 563-12-2
Last Revised — 03/31/1987

- 563-12-2
- AC 3422
- Bis(S-(Diethoxyphosphinothioyl)Mercapto)Methane
- Bladan
- Diethion
- Embathion
- ENT 24,105
- Ethanox
- Ethiol
- Ethiol 100
- Ethion
- Ethodan
- Ethopaz
- Ethyl Methylene Phosphorodithioate
- FMC-1240
- Fosfatox E
- Fosfono 50
- Hylemax
- Hylemox
- Itopaz

- KWIT
- NIA 1240
- Niagara 1240
- Nialate
- O,O,O,O-Tetraethyl S,S'-Methylenebis
- O,O,O',O'-Tetraethyl S,S'-Methylenebisphosphordithioate
- O,O,O',O'-Tetraethyl S,S'-Methylenebisphos-phorodithioate
- O,O,O',O'- Tetraethyl S,S'-Methylene Di(Phosphorodithioate)
- Phosphorodithioic Acid, S,S'-Methylene O,O,O',O'-Tetraethyl Ester
- Phosphotox E
- Rhodiocide
- Rhodocid
- Rodocid
- Rodocide
- RP 8167
- Soprathion
- S,S'-Methylene O,O,O',O'-Tetraethyl Phosphorodithioate
- Tetraethyl S,S'-Methylene Bis(Phosphorothiolothionate)
- Vegfru Fosmite