

Malathion; CASRN 121-75-5

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 [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 Malathion

File First On-Line 09/30/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/30/1987
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 — Malathion

CASRN — 121-75-5

Last Revised — 09/30/1987

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
RBC ChE depression	NOEL: 16 mg/day (0.23 mg/kg/day)	10	1	2E-2 mg/kg/day
Subchronic Human Feeding Study	LEL: 24 mg/day (0.34 mg/kg/day)			
Moeller and Rider, 1962				

*Conversion Factors and Assumptions — Adult human male body weight = 70\kg

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

Moeller, H.C. and J.A. Rider. 1962. Plasma and red blood cell cholinesterase activity as indications of the threshold of incipient toxicity of ethyl-p- nitrophenyl thionobenzenephosphorate (EPN) and malathion in human beings. *Toxicol. Appl. Pharmacol.* 4: 123-130.

Malathion was administered by gelatin capsules to groups of five healthy male volunteers ranging in age from 23-63 years at doses of either 8 mg/day for 32 days, 16 mg/day for 47 days, or 24 mg/day for 56 days. Cholinesterase activity was determined twice weekly before, during, and after administration of the chemical. The intermediate dose was a NOEL. The high dose was associated with a depression in plasma and RBC cholinesterase activity with no clinically manifested side effects.

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

UF — An uncertainty factor of 10 was used to account for the range of sensitivity within the human population.

MF — None

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

Data Considered for Establishing the RfD:

- 1) 47-Day Feeding - human: Principal study - see previous description; no core grade
- 2) 2-Year Feeding/Oncogenic - rat: Systemic NOEL=100 ppm (5 mg/kg/day); Systemic LEL=1000 ppm (50 mg/kg/day) (decreased brain cholinesterase and body weight); core grade minimum (American Cyanamid Co., 1980)
- 3) Reproduction - rat: Reproductive NOEL=none; LEL=240 mg/kg/day (only dose tested; reduced number of live pups and reduced pup body weight) (Kalow and Marton, 1961)
- 4) Teratology - rat: (i.p. injection) Reproductive NOEL and Terata NOEL=900 mg/kg/day; LEL=none (Kimbrough and Gaines, 1968)
- 5) 4-Week Inhalation - dog: NOEL=none; LEL=5 ppm (one dose and one dog tested) (Anonymous, 1965)

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

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Medium
RfD — Medium

The principal study is of fair quality and is given a medium confidence rating. The database supports the choice of the human cholinesterase NOEL as the basis of the RfD, but since the database on chronic toxicity is incomplete, it 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 Files

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

Verification Date — 03/18/1987

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 Malathion conducted in September 2002 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 — Malathion

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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Malathion

CASRN — 121-75-5

Not available at this time.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Malathion

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VI.A. Oral RfD References

American Cyanamid Company. 1980. MRID No. 00110562; HED Doc. No. 002504. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Anonymous. 1965. FAO/WHO Report. HED Doc. No. 000316, 000389. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Kalow, W. and A. Marton. 1961. Second-generation toxicity of malathion in rats. *Nature* (London). 192: 464-465.

Kimbrough, R. and T. Gaines. 1968. Effect of organic phosphorus compounds and alkylating agents on the rat fetus. *Arch. Environ. Health*. 16(Jun.): 805-808.

Moeller, H.C. and J.A. Rider. 1962. Plasma and red blood cell cholinesterase activity as indications of the threshold of incipient toxicity of ethyl-p- nitrophenyl thionobenzenephosphate (EPN) and malathion in human beings. *Toxicol. Appl. Pharmacol.* 4: 123-130.

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

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

VIII. Synonyms

Substance Name — Malathion
CASRN — 121-75-5
Last Revised — 09/30/1987

- 121-75-5
- American Cyanamid 4,409
- Cabofos
- Calmathion
- Carbethoxy Malathion
- Carbetox
- Carbophos
- Chemathion
- Cythion
- Detmol MA 96%
- Dicarboethoxyethyl O,O-Dimethyl Phosphorodithioate
- 1,2-Di(Ethoxycarbonyl)Ethyl O,O-Dimethyl Phosphorodithioate
- Diethyl Mercaptosuccinate, O,O-Dimethyl Dithiophosphate, S-Ester
- Diethyl Mercaptosuccinate, O,O-Dimethyl Phosphorodithioate
- Diethyl Mercaptosuccinate, O,O-Dimethyl Thiophosphate
- Dithiophosphate de O,O-Dimethyle et de S-(1,2-Dicarboethoxyethyle)
- Emmatos Extra
- ENT 17,034
- Ethiolacar

- Formal
- Fosfotion
- Fosfotion
- Fyfanon
- Karbofos
- Kop-thion
- Kypfos
- Malacide
- Malagran
- Malakill
- Malamar
- Malamar 50
- Malaphele
- Malaphos
- Malaspray
- Malathion
- Malathon
- Malation
- Malatol
- Malatox
- Maldison
- Malmed
- Malphos
- Maltox
- Mercaptothion
- Mercaptotion
- MLT
- NCI-C00215
- Oleophosphothion
- O,O-Dimethyldithiophosphate Diethylmercaptosuccinate
- O,O-Dimethyl S-(1,2-Bis(Ethoxycarbonyl)Ethyl)Dithiophosphate
- O,O-Dimethyl-S-(1,2-Dicarbethoxyethyl) Dithiophosphate
- O,O-Dimethyl S-(1,2-Dicarbethoxyethyl)Phosphorodithioate
- O,O-Dimethyl S-(1,2-Dicarbethoxyethyl)Thiothionphosphate
- O,O-Dimethyl S-1,2-Di(Ethoxycarbonyl)Ethyl Phosphorodithioate
- O,O-Dimethyl-S-1,2-Dikarbetoxyethylthiofosfat
- Phosphothion
- Sadofos
- Sadophos
- S-(1,2-Bis(Aethoxy-Carbonyl)-Aethyl)-O,O-Dimethyldithiophosphat
- S-(1,2-Bis(Ethoxy-Carbonyl)-Ethyl)-O,O-Dimethyldithiofosfaat
- S-(1,2-Bis(Ethoxycarbonyl)Ethyl O,O-Dimethyl Phosphorodithioate
- S-1,2-Bis(Ethoxycarbonyl)Ethyl-O,O-Dimethyl Thiophosphate
- S(1,2-Bis(Etossi-Carbonil)-Etil)-O,O-Dimetil-Ditiofosfato
- S-(1,2-Di(Ethoxycarbonyl)Ethyl Dimethyl Phosphorothiolothionate

- SF 60
- Siptox 1
- Sumitox
- Vegfru
- Zithiol