Methamidophos; CASRN 10265-92-6

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 <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 Methamidophos

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)

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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

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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	NOEL: none	1000	1	5E-5 mg/kg/day
One-Year Dog Feeding Study	LEL: 2 ppm diet (0.05 mg/kg/day)			
Mobay Chemical, 1984a				

*Conversion Factors -- 1 ppm = 0.025 mg/kg/day (assumed dog food consumption)

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

Mobay Chemical Corporation. 1984a. MRID No. 00147938, 41234304. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Beagle dogs were divided into groups of 6/sex/dose and fed the following levels of methamidophos: 0, 2, 8, or 32 ppm. The animals were treated for 1 year and appropriate tests were conducted. No treatment-related effects were observed (with the exception of cholinesterase inhibition) in clinical chemistry, hematology, and urinalysis studies; in clinical signs, body weights, organ weights, and food consumption; or in histopathologic and opthalmologic examinations. Inhibition of cholinesterase activities was noted in plasma, RBC, and brain at all levels.

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

UF — An uncertainty factor of 1000 was used to account for inter- and intraspecies differences, and for the fact that a NOEL was not established for any ChE endpoint.

MF — None

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

Data Considered for Establishing the RfD:

1) 1-Year Feeding - dog: Principal study - see previous description; core grade guideline

2) 2-Generation Reproduction - rat: Reproductive NOEL=none (Compound-related decreases in percentage of sperm-positive females delivering litters at all dose levels (0.15, 0.5 and 1.65 mg/kg/day); Systemic NOEL=10 ppm (0.5 mg/kg/day), Systemic LEL=33 ppm (1.65 mg/kg/day) (reduced body weights during premating period); core grade supplementary (Mobay Chemical, 1984b)

3) 2-Year Feeding (oncogenic) - rat: Systemic NOEL=0.3 mg/kg/day; ChE LEL=0.1 mg/kg/day (erythrocytes, plasma, brain); core grade minimum (Mobay Chemical, 1984c)

4) Teratology - rat: Teratogenic NOEL=3 mg/kg/day (HDT); LEL=none; Maternal and Fetotoxic NOEL=1 mg/kg/day; Maternal and Fetotoxic LEL=3 mg/kg/day (decreased body weights; clinical signs typical of cholinesterase inhibitors); core grade minimum (Mobay Chemical, 1984d)

5) Teratology - rabbit: Teratogenic and Fetotoxic NOEL=2.5 mg/kg/day (HDT); LEL=none; Maternal LEL=0.1 mg/kg/day (LDT; decreased body weight gain) (Mobay Chemical, 1979)

Data Gap(s): Rat Reproduction Study (Repeat to establish a NOEL); Brain Cholinesterase Study with Dogs; Brain Cholinesterase Study with Rats

I.A.5. Confidence in the Oral RfD

Study — High Database — Medium RfD — Medium

The biological effect upon which the RfD is based is debatable in terms of the extent to which this effect is biologically significant. The chosen study is well-conducted and is given a high confidence rating. Other studies of good quality on this chemical are available; however, the rat chronic study also indicates a ChE inhibition at all dose levels tested, and the reproductive study also needs a NOEL. Thus, 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 Files

Agency Work Group Review — 08/05/1986, 05/20/1987

Verification Date — 05/20/1987

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 Methamidophos 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 <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 — Methamidophos CASRN — 10265-92-6

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Methamidophos CASRN — 10265-92-6

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 — Methamidophos CASRN — 10265-92-6

VI.A. Oral RfD References

Mobay Chemical Corporation. 1979. MRID No. 00041315. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Corporation. 1984a. MRID No. 00147938, 41234304. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Corporation. 1984b. MRID No. 00148455, 41234301. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Corporation. 1984c. MRID No. 00148452, 41234301. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Mobay Chemical Corporation. 1984d. MRID No. 00148454. 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 — Methamidophos CASRN — 10265-92-6

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

VIII. Synonyms

Substance Name — Methamidophos CASRN — 10265-92-6 Last Revised — 09/30/1987

- 10265-92-6
- ACEPHATE-MET
- BAY 71628
- BAYER 71628
- CHEVRON 9006
- ENT 27,396
- HAMIDOP
- METAMIDOFOS ESTRELLA
- Methamidophos
- MONITOR
- MTD
- NSC 190987
- ORTHO 9006
- O,S-DIMETHYL ESTER AMIDE of AMIDOTHIOATE
- O,S-DIMETHYL PHOSPHORAMIDOTHIOATE
- PHOSPHORAMIDOTHIOIC ACID, O,S-DIMETHYL ESTER
- PILLARON
- SRA 5172
- TAHMABON
- TAMARON
- THIOPHOSPHORSAEURE-O,S-DIMETHYLESTERAMID