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## Thiophanate-methyl; CASRN 23564-05-8

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 Thiophanate-methyl

**File First On-Line 01/31/1987**

| Category (section)                      | Assessment Available? | Last Revised |
|---|-----------------------|--------------|
| <b>Oral RfD (I.A.)</b>                  | yes                   | 01/31/1987   |
| <b>Inhalation RfC (I.B.)</b>            | not evaluated         |              |
| <b>Carcinogenicity Assessment (II.)</b> | not evaluated         |              |

### I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

#### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Thiophanate-methyl

CASRN — 23564-05-8

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               |
|---|--------------------------------|-----|----|-------------------|
| <b>Decreased body weight, decreased spermatogenesis, and histological evidence of hyperthyroidism</b> | NOEL: 160 ppm<br>(8 mg/kg/day) | 100 | 1  | 8E-2<br>mg/kg/day |
|   | LEL: 640 ppm<br>(32 mg/kg/day) |     |    |                   |
| <b>2-Year Rat Feeding Study</b>   |                                |     |    |                   |
| <b>Pennwalt Corp., 1972a</b>  |                                |     |    |                   |

\*Dose Conversion Factors & Assumptions: 1 ppm = 0.05 mg/kg/day (rat food consumption)

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

Pennwalt Corporation. 1972a. MRID No. 00032673, 00117868; HED Doc. No. 00200, 00203, 004260. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Four groups consisting of 35 male and 35 female SPF. Sprague-Dawley rats were given diets containing 10, 40, 160, or 640 ppm of thiophanate-methyl. A control group of 50 males and 50 females was included. The animals were checked daily for toxic signs and mortality. Body weight and food consumption were recorded. Hematologic and clinical chemistry testing, and blood analysis were performed periodically. At sacrifice, organ weight and histopathologic changes were also reported. The systemic NOEL was 160 ppm (8 mg/kg/day), and the LEL was 640 ppm (32 mg/kg/day). The treatment caused growth retardation, decreased spermatogenesis, and histologic evidence of hyperthyroidism.

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

UF — A 100-fold uncertainty factor has been used to compensate for the inter- and intraspecies differences in extrapolating from rats to humans.

MF — None

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

Another reproduction study available was concerned only with effects on the male reproductive system. No effects were found at 195 mg/kg thiophanate- methyl, although there was an observed increase in adrenal weights (core grade minimum).

##### Data Considered for Establishing the RfD

- 1) 2-Year Feeding (Oncogenic) - rat: Principal study - see discussion above; core grade minimum
- 2) 2-Year Feeding - dog: NOEL=50 mg/kg/day; LEL=250 mg/kg/day (growth retardation, elevated thyroid weight); core grade minimum (Pennwalt Corp., 1972b)
- 3) Teratology - rat: Teratogenic NOEL=2500 ppm (125 mg/kg/day) (HDT); Maternal NOEL=250 ppm (12.5 mg/kg/day), LEL=1200 ppm (60 mg/kg/day); Fetotoxic NOEL=2500 ppm (HDT); core grade minimum (Atochem North America, Inc., 1985)
- 4) Teratology - mice: The 1000 mg/kg/day dose caused decreased number of implantations; core grade supplementary (Incomplete descriptions of protocol, fetal examinations did not appear to include soft tissue examinations) (Pennwalt Corp., 1970a)
- 5) 3-Generation Reproduction - rat: Reproductive NOEL=160 ppm (8 mg/kg/day); LEL=640 ppm (32 mg/kg/day) (HDT) (reduced litter weights); core grade minimum (Pennwalt Corp., 1970c)

##### Other Data Reviewed

- 1) 2-Year Feeding (Oncogenic) - Mice: Systemic NOEL=160 ppm (22.85 mg/kg/day); core grade minimum (Pennwalt Corp., 1970b)

Data Gap(s): Rabbit Teratology Study

#### **I.A.5. Confidence in the Oral RfD**

Study — High  
Database — High  
RfD — High

The principal study appears to be of high quality and is given a high rating. The database is very supportive, but has one data gap; therefore, confidence in the database can be considered high to medium. Confidence in the RfD can also be considered high to medium.

#### **I.A.6. EPA Documentation and Review of the Oral RfD**

Pesticide Registration Files

Agency Work Group Review — 03/11/1986

Verification Date — 03/11/1986

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 Thiophanate-methyl 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](mailto: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](mailto:hotline.iris@epa.gov) (internet address).

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

Substance Name — Thiophanate-methyl  
CASRN — 23564-05-8

Not available at this time.

## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Thiophanate-methyl  
CASRN — 23564-05-8

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

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## **VI. Bibliography**

Substance Name — Thiophanate-methyl  
CASRN — 23564-05-8

### **VI.A. Oral RfD References**

Atochem North America, Inc. 1985. MRID No. 00146643, 92186011; HED Doc. No. 004459. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Pennwalt Corporation. 1970a. MRID No. 0055937; HED Doc. No. 00200, 004260. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Pennwalt Corporation. 1970b. MRID No. 00081611; HED Doc. No. 00200, 00203, 00206, 004260. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Pennwalt Corporation. 1972a. MRID No. 00032673, 00117868; HED Doc. No. 00200, 00203, 004260. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Pennwalt Corporation. 1972b. MRID No. 00055930, 00057652, 00080282, 00117869; HED Doc. No. 00200, 00203, 004260. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Pennwalt Corporation. 1972c. MRID No. 00055931, 00117870, 00057653; HED Doc. No. 00203, 004260. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

### **VI.B. Inhalation RfC References**

None

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### VI.C. Carcinogenicity Assessment References

None

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### VII. Revision History

Substance Name — Thiophanate-methyl  
CASRN — 23564-05-8

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

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### VIII. Synonyms

Substance Name — Thiophanate-methyl  
CASRN — 23564-05-8  
Last Revised — 01/31/1987

- 23564-05-8
- ALLOPHANIC ACID, 4,4'-o-PHENYLENEBIS(3-THIO-, DIMETHYL ESTER
- BAS 32500F
- 1,2-BIS(METHOXYCARBONYLTHIOUREIDO)BENZENE
- 1,2-BIS(3-(METHOXYCARBONYL)-2-THIOUREIDO)BENZENE
- o-BIS(3-METHOXYCARBONYL-2-THIOUREIDO)BENZENE
- CARBAMIC ACID, (1,2-PHENYLENEBIS(IMINOCARBONOTHIOYL))BIS-, DIMETHYL ESTER

- CERCOBIN M
- CERCOBIN METHYL
- DIMETHYL ((1,2-PHENYLENE)BIS-(IMINOCARBONOTHIOYL))BIS(CARBAMATE)
- DIMETHYL-4,4'-o-PHENYLENE-BIS-(3-THIOALLOPHANATE)
- ENOVIT M
- ENOVIT METHYL
- ENOVIT-SUPPER
- FRUMIDOR
- FUNGITOX
- FUNGO
- FUNGO 50
- LABILITE
- METHYLTHIOFANATE
- METHYL THIOPHANATE
- METHYL TOPSIN
- MILDOTHANE
- NEOTOPSIN
- NF 44
- PELT 14
- PELT-44
- SIGMA
- SIPCAPLANT
- SIPCASAN
- SIPCAVIT
- TD 1771
- THIOPHANATE M
- Thiophanate-methyl
- TIOFANATE METILE
- TOPSIN M
- TOPSIN NF-44
- TOPSIN WP METHYL
- TREVIN
- ZYBAN