

Phenmedipham; CASRN 13684-63-4

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 Phenmedipham

File First On-Line 06/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	06/01/1990
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 — Phenmedipham
CASRN — 13684-63-4
Primary Synonym — Betanal
Last Revised — 06/01/1990

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
No adverse effects	NOAEL: 500 ppm (25 mg/kg/day)	100	1	2.5E-1 mg/kg/day
2-Year Rat Feeding/ Carcinogenicity Study	LEL: None			
Nor-Am Agricultural Products, Inc., 1980a				

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

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

Nor-Am Agricultural Products, Inc. 1980a. MRID No. 0028651. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Albino rats (60/sex/dose group) were administered 0, 20, 100, and 500 ppm (0, 1, 5, and 25 mg/kg/day) of phenmedipham in the diet for 104 weeks. All animals were observed twice daily for mortality. Individual body weight and food consumption were recorded weekly for the first 13 weeks and once a week thereafter. External observations of gross signs of toxicity and pharmacologic effects, and the incidence, size, and location of tumors were recorded at the same intervals. Hematology, clinical chemistry, and urinalysis (pooled samples) were performed on 5 animals/sex/dose group at weeks 13, 26, 52, 78, and 104. At the same intervals, cholinesterase studies were performed on 10 additional animals of each sex from the control and high-dose group. Blood samples for hematology were evaluated for hematocrit, hemoglobin, erythrocyte and total leukocyte count and differential leukocyte count serum samples were evaluated for SGOT, alkaline phosphatase, total bilirubin, blood urea nitrogen, fasting blood glucose, total protein, and total albumin/globin ratio. Brain cholinesterase determinations were made from 10 male and 10 female animals from the control and high-dose group at week 104. Following 52

weeks of treatment, 10 animals/sex/dose were sacrificed and necropsied. Terminal necropsies were performed on all animals following week 104 on all surviving animals.

A total of 60 male (19 control, 12 low-dose, 17 mid-dose, and 12 high-dose) and 67 female (13 control, 15 low-dose, 17 mid-dose, and 22 high-dose) animals died during the study. No distinct or consistent treatment related clinical signs were observed in any of the treatment groups. The mean body weights of the low- and mid-dose groups were comparable to control values throughout the study. At the high-dose there was a minimal (<10%) depression of female mean body weight gain. No significant differences in food consumption between control and compound treated animals were noted.

The NOAEL for systemic toxicity is greater than or equal to 500 ppm (25 mg/kg/day) (HDT). A LEL for systemic toxicity was not established in this study.

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

UF — An uncertainty factor of 100 was used to account for the inter- and intraspecies differences.

MF — None

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

Data Considered for Establishing the RfD

1. 2-Year Feeding (carcinogenicity) - rat: see previous description core grade supplementary
2. 2-Year Feeding - dog: Dietary levels tested: 0, 40, 200, and 1000 ppm (0, 1, 5, and 25 mg/kg/day); Beagle dogs were dosed orally (mixed in the diet) for 104 weeks. Eight animals/sex were used in each dose group and a control. No significant effects were observed at any dose tested. Therefore, the NOEL is greater than or equal to 1000 ppm (25 mg/kg/day) (HDT); core grade minimum (Nor-Am Agricultural Products, Inc., 1980b)
3. 3-Generation Reproduction - rat: Dietary levels tested: 0, 20, 100, and 500 ppm (0, 1, 5, and 25 mg/kg/day); 15 male and 30 female rats were used at the start of the study per dose group and a control. This study examined 3 generations, 2 litters per generation, and a teratology phase (P1-F1a generation). No significant effects were observed at any dose level. Therefore, the NOEL for reproductive toxicity is greater than or equal to 500 ppm (25 mg/kg/day) (HDT); core grade minimum (Nor-Am Agricultural Products, Inc., 1979)
4. Teratology - rat: Dietary levels tested: 0, 20, 100, and 500 ppm (0, 1, 5, and 25 mg/kg/day). This study was a part of the rat reproduction study. Fifteen dams were used per group of the P1-F1a generation. No significant effects were observed at any dose

level. Therefore, the NOEL for Developmental toxicity is greater than or equal to 500 ppm (25 mg/kg/day) (HDT); core grade supplementary (Nor-Am Agricultural Products, Inc., 1979)

5. Data Gap(s): Chronic Rat Feeding Study; Rat Developmental Toxicity Study (new study is under review); Rabbit Developmental Toxicity Study

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — Medium

RfD — Medium

Since no signs of toxicity were observed at any dose level, confidence in the critical study can be considered medium to low. Although additional studies support the critical study, confidence in the database can also be considered medium to low because the studies did not provide a complete assessment of toxicity potential. Medium to low confidence in the RfD follows.

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, October 1986; Pesticide Registration Files

Agency Work Group Review — 03/21/1990

Verification Date — 03/21/1990

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 phenmedipham conducted in August 2003 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 — Phenmedipham

CASRN — 13684-63-4

Primary Synonym — Betanal

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Phenmedipham

CASRN — 13684-63-4

Primary Synonym — Betanal

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 — Phenmedipham

CASRN — 13684-63-4

Primary Synonym — Betanal

VI.A. Oral RfD References

Nor-Am Agricultural Products, Inc. 1979. MRID No. 00027482. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Nor-Am Agricultural Products, Inc. 1980a. MRID No. 0028651. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Nor-Am Agricultural Products, Inc. 1980b. MRID No. 00028650, 00081232. 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 — Phenmedipham

CASRN — 13684-63-4

Primary Synonym — Betanal

Date	Section	Description
06/01/1990	I.A.	Oral RfD summary on-line
10/28/2003	I.A.6	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Phenmedipham

CASRN — 13684-63-4

Primary Synonym — Betanal

Last Revised — 06/01/1990

- 13684-63-4
- Carbamic acid, (3-methylphenyl)-, 3-((methoxycarbonyl)amino)phenyl ester
- Betanal
- Carbanilic acid, m-hydroxy-, methyl
- Caswell No. 648B
- EP 452
- EP-452
- EPA Pesticide Chemical Code 098701
- Fenmedifam
- HSDB 1402
- Methyl m-hydroxycarbanilate m-methylcarbanilate
- Methyl m-hydroxycarbanilate m-methylcarbanilate
- METHYL m-HYDROXYCARBANILATE, m-METHYLCARBANILATE
- METHYL N-(3-(N-(3-METHYLPHENYL)CARBAMOYLOXY) PHENYL)CARBAMATE
- Methyl 3-(3-methylcarbaniloxy)carbanilate
- Morton EP 452
- Phenmedipham
- Phenmediphame [ISO-French]
- S 4075
- Schering 4072
- SCHERING-38584
- SN 38584
- SN 4075
- SN-38584
- 3-((Methoxycarbonyl)amino)phenyl (3-methylphenyl)carbamate
- 3-((METHOXYCARBONYL)AMINO)PHENYL N-(3-METHYLPHENYL)CARBAMATE
- 3-(CARBOMETHOXYAMINO)PHENYL 3-METHYLCARBANILATE
- 3-METHOXYCARBONYL-N-(3'-METHYLPHENYL)-CARBAMAT [German]
- 3-METHOXYCARBONYLAMINOPHENYL N-3'-METHYLPHENYLCARBAMATE
- 3-Methoxycarbonylaminophenyl 3'-methylcarbanilate