

Propargite; CASRN 2312-35-8

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 Propargite

File First On-Line 05/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	05/01/1990
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 — Propargite
CASRN — 2312-35-8
Primary Synonym — Omite
Last Revised — 05/01/1990

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 observed at the HDT	NOEL: 900 ppm (22.5 mg/kg/day)	1000	1	2E-2 mg/kg/day
2 Year Dog Feeding Study	LEL: None			
Uniroyal Chemical, 1966				
Reduced body weight gain; increased resorption; reduced body weight; delayed ossification	NOEL: 2.0 mg/kg/day (Maternal and Fetotoxic) LEL: 6.0 mg/kg/day (Maternal and Fetotoxic)	100	1	2E-2 mg/kg/day
Rabbit Developmental Toxicity Study				
Uniroyal Chemical, 1982				

*Conversion Factors: 1 ppm = 0.025 mg/kg/day (assumed dog food consumption) Actual dose tested for the developmental toxicity study

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

Uniroyal Chemical. 1966. MRID No. 00076402. Uniroyal Chemical. 1982. MRID No. 00105990. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Four male and four female purebred beagle dogs were fed Omite for 2 years at 0, 100, 300, and 900 ppm (0, 2.5, 7.5, and 22.5 mg/kg/day) (Uniroyal Chemical, 1966). Growth and food intake were comparable to the control group. No adverse effects were observed by hematology, blood

chemistry determinations or urine examinations. Gross postmortem examination failed to reveal any dose-related effects. No significant microscopic changes in the tissues and organs were observed. The NOEL for systemic toxicity is equal to or greater than 900 ppm (22.5 mg/kg/day) (HDT).

The test material was administered orally by intubation from day 6 through day 18 of gestation to 4 groups of 17 pregnant female rabbits at dose levels of 2, 6, 10, and 18 mg/kg/day (Uniroyal Chemical, 1982). Test group dosages were prepared as a suspension in corn oil. Another group of 17 female pregnant rabbits served as control and received corn oil vehicle only. A dose-related pattern of decrease in body weight gain in females was noted at 6 mg/kg/day and above and was statistically significant in the highest group (18 mg/kg/day). Lower survival of pregnant and nonpregnant females was observed at 10 and 18 mg/kg/day. The fetuses showed delayed ossification at 6 mg/kg/day and above; this was considered related to maternal toxicity of the test compound. Fetotoxicity was also evidenced by increased resorptions and reduced fetal body weight at 6 mg/kg/day and reduced fetal viability at 10 and 18 mg/kg/day. Therefore, based on the above effects the NOEL for maternal toxicity and fetotoxicity is 2 mg/kg/day.

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 for the use of either the chronic dog or rabbit developmental NOELs. An additional UF of 10 was used on the dog NOEL to account for the uncertainties in the other chronic studies and uncertainties created by effects observed in the developmental toxicity studies, making uncertain the determination of the most sensitive toxicological endpoint.

MF — None

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

The NOELs for developmental effects in both rats and rabbits are lower than the dog NOEL also chosen to establish the RfD. However, the developmental toxicity studies are difficult to interpret because of the irritating properties of the chemical and the gavage nature of the exposure. Thus, the work group felt the need to list both the chronic dog study and the rabbit developmental toxicity study as co-critical. Identical RfDs are derived.

Data Considered for Establishing the RfD

1) 2-Year Feeding - dog: Principal study - see previous description; core grade minimum (Uniroyal Chemical, 1966)

2) Developmental toxicity - rabbit: Co-critical study - see previous description; core grade minimum (Uniroyal Chemical, 1982)

3) 2-Year Feeding (oncogenic) - rat: Dietary levels tested: 0, 100, 300, 900, and 2000 ppm (0, 5, 15, 45, 100 mg/kg/day); Twenty-five male and 25 female weanling rats of the FDRL strain were fed propargite at 0, 100, 300 and 900 ppm for 2 years and 2000 ppm for 1.5 years. Fifteen rats/sex were used as controls. No dose-related responses were disclosed by hematology, blood chemistry determinations, or urinalysis. Scattered instances of lower mean body weight gains at weeks 26 through 104 were noted in females receiving diets of 100, 300, and 900 ppm when compared with control values. However, the mean body weight gain for females in all treated groups was about 6% reduced to 104 weeks of the study when compared with the control values which appears not to be statistically significant. At 74 weeks the mean body weights of rats fed 2000 ppm (HDT) was significantly reduced for both males and females. This group also consumed less food and had a lower mean body weight gain when compared with the control group. The LEL for systemic toxicity is 2000 ppm (100 mg/kg/day) based on significantly reduced mean body weights. Therefore, the NOEL for systemic toxicity is 2000 ppm (45 mg/kg/day) (HDT); core grade supplementary (Uniroyal Chemical, 1966)

4) 3-Generation Reproduction - rat: Dietary levels tested: 0, 100, and 300 ppm (0, 5, and 15 mg/kg/day); Groups of 25 male and 25 female rats were fed 0 or 100 ppm for one generation. The dose of the treatment group was then increased to 300 ppm for the next two generations. The study results revealed no significant effects on either fertility or reproductive performance. Neonatal viability and lactation efficiency as evidenced by the survival and growth of the young rats from birth to weaning were comparable with the control group. Mean body weight of the pups was also comparable with that of the control group. The NOEL for reproductive toxicity is equal to or greater than 300 ppm (15 mg/kg/day) (HDT); core grade supplementary (Uniroyal Chemical, 1966)

5) Developmental toxicity - rat: Dietary levels tested: 0, 6, 25, and 105 mg/kg/day; propargite was administered by gavage to pregnant rats from day 6 through day 15 of gestation. An increase in mortality was observed in parental animals at 105 mg/kg/day (HDT). Therefore, the NOEL and LEL for maternal toxicity are 25 and 105 mg/kg/day, respectively. An increased incidence of missing sternebrae was observed at 25 mg/kg/day. Therefore, the NOEL and LEL for fetotoxicity are 6 and 25 mg/kg/day, respectively. No teratogenic effects were noted at any dose tested; core grade minimum (Uniroyal Chemical, 1979a)

Other Data Reviewed:

1) 18-Month Feeding (carcinogenicity - mouse: Dietary levels tested: 0, 50, 160, 500, and 1000 ppm (0, 7.5, 24, 75, and 150 mg/kg/day); 60 male and 60 female albino CD-1 mice/dose group

were administered propargite for 18 months. Observations of the animals daily for 18 months revealed no untoward effects toward food consumption, body weights, hematology, and survival. Variable organ weight changes in the kidney, adrenal, and uterus were not supported by any pathology in these organs. The NOEL for systemic is greater than or equal to 1000 ppm (150 mg/kg/day) (HDT); core grade minimum (Uniroyal Chemical, 1979b)

2) 90-day Feeding - dog: Dietary levels tested: 2000 to 2500 ppm (0, 50 to 62.5 mg/kg/day); Male and female beagle dogs were administered propargite at a dietary level from 2000 to 2500 ppm for 90 days. Signs of apparent compound effects among the test dogs were decreased appetite and body weight loss. The test animals were comparable with the controls in appearance, behavior, elimination, results of clinical laboratory studies, organ weights, organ/body weight ratios, and gross necropsy findings. The NOEL for systemic toxicity is less than 2000 ppm (50 mg/kg/day) based on decreased appetite and body weight loss; core grade supplementary (Uniroyal Chemical, 1968)

3) 90-Day Feeding - rat: Dietary levels tested: 0, 10, 20, 40, 100, and 200 mg/kg/day; Propargite was administered to 5 groups of weanling albino rats consisting of 5 males and 5 females each for 90 days. A control group of 15 males and 15 females was used and received no treatment. Clinical examination including hematological and blood chemistry examinations disclosed no abnormalities. Growth was retarded at the 100 mg/kg/day group and to a greater extent in the 200 mg/kg/day group. Marked reduction in absolute organ weights in the 200 mg/kg/day group was observed. Gross microscopic examination of liver, kidneys, adrenal, and gonads of the rats disclosed no significant abnormalities in any of the treated groups. The LEL for systemic toxicity is 100 mg/kg/day based on retarded growth. Therefore, the NOEL for systemic toxicity is 40 mg/kg/day; core grade minimum (Uniroyal Chemical, 1964)

Data Gap(s): Chronic Rat Feeding Study, Rat Reproduction Study

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — Medium

RfD — Medium

The critical studies are of adequate quality and are given medium confidence ratings. Because of the lack of two adequate chronic studies (rat feeding and reproduction studies), 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

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — Pesticide Registration Standard, April 1986; Pesticide Registration Files

Agency Work Group Review — 08/19/1986, 04/15/1987, 03/23/1988

Verification Date — 03/23/1988

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 propargite conducted in August 2003 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 — Propargite

CASRN — 2312-35-8

Primary Synonym — Omite

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Propargite

CASRN — 2312-35-8

Primary Synonym — Omite

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 — Propargite

CASRN — 2312-35-8

Primary Synonym — Omite

VI.A. Oral RfD References

Uniroyal Chemical. 1964. MRID No. 0007641. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical. 1966. MRID No. 00076402. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical. 1968. MRID No. 00036285. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical. 1979a. MRID No. 00041386. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical. 1979b. MRID No. 00130942. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical. 1982. MRID No. 00105990. 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 — Propargite

CASRN — 2312-35-8

Primary Synonym — Omite

Date	Section	Description
05/01/1990	1.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 — Propargite

CASRN — 2312-35-8

Primary Synonym — Omite

Last Revised — 05/01/1990

- 2312-35-8
- comite
- cyclosulfyne
- D014
- ENT 27226
- Naugatuck D014
- Omite
- omite 57 E
- omite 85 E
- propargil

- Propargite
- sulfurous acid, 2-[4-(1,1-dimethylethyl)phenoxy] cyclohexyl 2-propynyl ester
- sulfurous acid, 2-(p-tert-butylphenoxy)cyclohexyl 2-propynyl ester
- 2-(p-tert-butylphenoxy)cyclohexyl propargyl sulfite
- 2-(p-tert-butylphenoxy)cyclohexyl 2-propynyl sulfite
- Uniroyal D014