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Prometryn; CASRN 7287-19-6

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 [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 Prometryn

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 — Prometryn

CASRN — 7287-19-6

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 |
|--------------------------------------------------------------|----------------------------------------|------|----|-------------------|
| Liver and kidney degeneration and bone marrow atrophy | NOEL: 150 ppm diet (3.75 mg/kg/day) | 1000 | 1 | 4E-3 mg/kg/day |
| 106-Week Dog Feeding Study | LEL: 1500 ppm diet (37.5 mg/kg/day) | | | |
| Ciba-Geigy, 1965a | | | | |

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

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

Ciba-Geigy Corporation. 1965a. MRID No. 00042794; HED Doc. No. 001830, 003500, 005665, 005666. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Groups of 3 male and 3 female beagles were dosed with prometryn 80W (80% wettable powder) in their feed for 106 weeks at active ingredient (a.i.) concentration levels of 0 (vehicle control), 15, 150, and 1500 ppm (0, 0.375, 3.75, and 37.5 mg/kg/day). The dogs were observed daily, weighed weekly, given physical examinations daily for the first week and weekly thereafter, and given neurologic and ophthalmic examinations monthly. Food consumption was measured daily. The following clinical pathology measurements were made: Hematology - hematocrit, hemoglobin, sedimentation rate, and leukocytes (total and differential); Clinical Chemistry - BUN, glucose, alkaline phosphatase, and SGOT; Urinalysis - specific gravity, pH, albumin, sugar, appearance, and microscopic sediment. All surviving dogs were sacrificed at 106 weeks and examined grossly. A battery of tissues were examined histopathologically. The defined doses were as follows: NOEL = 3.75 mg a.i./kg/day (150 ppm a.i.); LEL = 37.5 mg a.i./kg/day (1500 ppm a.i.) - degenerative hepatic changes, renal tubule degeneration, and slight bone marrow atrophy.

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

UF — A 100-fold UF has been used to compensate for the inter- and intraspecies differences in extrapolating from the dog to the human. An additional UF of 10 was used because the existing database does not unequivocally establish that the dog is the most sensitive species. The other studies (each having a higher NOEL) are of insufficient quality.

MF — None

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

This chemical has a very old database. The RfD was established on the data available and given a low confidence.

Data Considered for Establishing the RfD:

- 1) 106-Week Feeding (80W) - dog: Principal study - see previous description; core grade minimum
- 2) 104-Week Feeding/Oncogenicity (50WP) - rat: Systemic NOEL=1250 ppm a.i. (62.5 mg a.i./kg/day, HDT); Systemic LEL=none; core grade supplementary (Ciba- Geigy, 1965b)
- 3) 3-Generation Reproduction (50WP) - rat: Reproductive NOEL=100 ppm a.i. (5.0 mg a.i./kg/day, HDT); LEL=none; core grade supplementary (Ciba-Geigy, 1966)
- 4) Teratogenicity (technical) - rabbit: Maternal NOEL=12 mg/kg/day; Maternal LEL=72 mg/kg/day (decreased food consumption-HDT); Embryotoxic NOEL=72 mg/kg/day; LEL=none; Fetotoxic NOEL=12 mg/kg/day; Fetotoxic LEL=72 mg/kg/day (increased fetal resorptions-HDT); Teratogenic NOEL=72 mg/kg/day (HDT); LEL=none; Developmental toxicity index=1; core grade minimum (Ciba-Geigy, 1985)
- 5) Teratogenicity - Rat NOEL and LEL values could not be defined with any degree of certainty because of the lack of individual animal data. There were reportedly no compound-related developmental anomalies at the HDT (250 mg/kg/day); core grade supplementary (Ciba-Geigy, 1977)

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

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

The principal study is old, but appears to be of satisfactory quality and is given a medium rating. The confidence in the database is low. Therefore, the confidence in the assigned RfD is low.

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

Pesticide Registration Standard (1986)

Pesticide Registration Files

Agency Work Group Review — 12/09/1986, 04/15/1987

Verification Date — 04/15/1987

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 prometryn 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 — Prometryn
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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Prometryn
CASRN — 7287-19-6

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 — Prometryn
CASRN — 7287-19-6

VI.A. Oral RfD References

Ciba-Geigy Corporation. 1965a. MRID No. 00042794; HED Doc. No. 001830, 003500, 005665, 005666. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1965b. MRID No. 00042794; HED Doc. No. 001830, 003500, 005665, 005666. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1966. MRID No. 00024472; HED Doc. No. 001830, 003500, 005665, 005666. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1977. MRID No. 00060644, 40457516; HED Doc. No. 001832, 005666. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1985. MRID No. 00157995; HED Doc. No. 005665, 005666. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Prometryn

CASRN — 7287-19-6

| Date | Section | Description |
|------------|---------|--------------------------------------------------------------------|
| 10/28/2003 | I.A.6 | Screening-Level Literature Review Findings message has been added. |

VIII. Synonyms

Substance Name — Prometryn

CASRN — 7287-19-6

Last Revised — 09/30/1987

- 7287-19-6
- 2,4-BIS(ISOPROPYLAMINO)-6-METHYL MERCAPTO-s-TRIAZINE
- 2,4-BIS(ISOPROPYLAMINO)-6-METHYLTHIO-1,3,5-TRIAZINE
- 2,4-BIS(ISOPROPYLAMINO)-6-METHYLTHIO-s-TRIAZINE
- 2,4-BIS(PROPYLAMINO)-6-METHYLTHIO-1,3,5-TRIAZIN
- CAPAROL
- G 34161
- GESAGARD
- MERKAZIN
- 2-METHYLMERCAPTO-4,6-BIS(ISOPROPYLAMINO)-s-TRIAZINE
- 2-METHYLTHIO-4,6-BIS(ISOPROPYLAMINO)-s-TRIAZINE
- N,N'-BIS(1-METHYLETHYL)-6-METHYL-THIO-1,3,5-TRIAZINE-2,4-DIAMINE

- POLISIN
- PRIMATOL Q
- PROMETREX
- PROMETRIN
- Prometryn
- PROMETRYNE
- SELEKTIN
- SESAGARD
- s-TRIAZINE, 4,6-BIS(ISOPROPYLAMINO)-2-METHYLMERCAPTO-
- s-TRIAZINE, 2,4-BIS(ISOPROPYLAMINO)-6-(METHYLTHIO)-

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