Ametryn; CASRN 834-12-8

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 Ametryn

File First On-Line 09/30/1987

<table>
<thead>
<tr>
<th>Category (section)</th>
<th>Assessment Available?</th>
<th>Last Revised</th>
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<tr>
<td>Oral RfD (I.A.)</td>
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<td>09/30/1987</td>
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<tr>
<td>Inhalation RfC (I.B.)</td>
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<tr>
<td>Carcinogenicity Assessment (II.)</td>
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I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Ametryn
CASRN — 834-12-8
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

<table>
<thead>
<tr>
<th>Critical Effect</th>
<th>Experimental Doses*</th>
<th>UF</th>
<th>MF</th>
<th>RfD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver toxicity</td>
<td>NOEL: 10 mg/kg/day</td>
<td>1000</td>
<td>1</td>
<td>9E-3 mg/kg/day</td>
</tr>
<tr>
<td></td>
<td>(converted to 8.6 mg/kg/day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat Subchronic Oral</td>
<td>LEL: 100 mg/kg/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(converted to 86 mg/kg/day)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*Conversion Factors and Assumptions — Dose adjusted for treatment schedule (6 days/week).

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


Rats were dosed with 0, 10, or 100 mg/kg/day ametryn by water gavage, 6 days/week for 13 weeks. The LEL of 100 mg/kg/day is associated with fatty degeneration of the liver. No effects were observed at 10 mg/kg/day. The study appears to have been well-conducted, with 12 males and 12 female rats in each of the two dose groups.

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

UF — An uncertainty factor of 1000 was used to account for the inter- and intraspecies differences, and to account for the subchronic duration of the critical study.

MF — None
I.A.4. Additional Studies/Comments (Oral RfD)

Although a rat teratology study had a NOEL of 5 mg/kg/day, it was not used to establish the RfD for the following reasons: 1) The exposure in the teratology study was by gavage, thus exaggerating internal dose when compared with dietary exposures; 2) the NOEL of the rat study used to establish the RfD is not significantly different from the NOEL in the teratology study; and 3) the effects noted at 50 mg/kg/day in the teratology study were minimal and of marginal biological significance.

Data Considered for Establishing the RfD:

1) 90-Day Feeding - rat: Principal study - see previous description

2) 4-Week Feeding (Range Finding) - rat: NOEL=100 mg/kg/day; LEL=250 mg/kg/day (decrease in body weight and bloody nasal secretion) (Ciba-Geigy, 1987a)

3) 90-Day Feeding - dog: NOEL=25 mg/kg/day (Ciba-Geigy, 1961b)

4) Reproduction - rat: NOEL=10 mg/kg/day; LEL=100 mg/kg/day (body weight loss) (Ciba-Geigy, 1987b)

5) Teratology - rat: Maternal and Fetotoxic NOEL=5 mg/kg/day; Maternal and Fetotoxic LEL=50 mg/kg/day (reduction in food consumption and body weight, hypoactivity, elevated forepaw metacarpals not ossified, and increase in salivation and ptosis) (Ciba-Geigy, 1985a)

6) Teratology - rabbit: Maternal NOEL=10 mg/kg/day; Fetotoxic NOEL=60 mg/kg/day (HDT); Maternal LEL=60 mg/kg/day [weight loss (gestational days 7-10)] (Ciba-Geigy, 1985b)

Data Gap(s): Chronic Dog Feeding Study; Chronic Rat Feeding Study; Rat Reproduction Study (in Progress)

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

The principal study is of fair quality and is given a medium confidence rating. The confidence in the database is low due to the fact that the database on chronic toxicity is incomplete and,
therefore, the most sensitive toxicologic endpoint cannot be determined. Low confidence in the 
RfD follows.

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

Pesticide Registration Files

Agency Work Group Review — 05/31/1985, 12/16/1987, 02/18/1987

Verification Date — 02/18/1987

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 Ametryn conducted in 
September 2002 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 — Ametryn
CASRN — 834-12-8

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ametryn
CASRN — 834-12-8

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 — Ametryn
CASRN — 834-12-8

VI.A. Oral RfD References


VII. Revision History

Substance Name — Ametryn  
CASRN — 834-12-8

<table>
<thead>
<tr>
<th>Date</th>
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<td>Screening-Level Literature Review Findings message has been added.</td>
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VIII. Synonyms

Substance Name — Ametryn  
CASRN — 834-12-8  
Last Revised — 09/30/1987

- 834-12-8
- A 1093
- AMETREX
- Ametryn
- AMETRYNE
- CARBAMIC ACID, METHYL-, o-ISOPROPOXYPHENYL ESTER
- CRISATRINE
- 2-ETHYLAMINO-4-ISOPROPYLAMINO-6-METHYLMERCAPTO-s-TRIAZINE
- 2-ETHYLAMINO-4-ISOPROPYLAMINO-6-METHYLTHIO-1,3,5-TRIAZINE
- 2-ETHYLAMINO-4-ISOPROPYLAMINO-6-METHYLTHIO-s-TRIAZINE
- EVIK
- G-34162
- GESAPAX
- 2-METHYLMERCAPTO-4-ETHYLAMINO-6-ISOPROPYLAMINO-S-TRIAZINE
- 2-METHYLMERCAPTO-4-ISOPROPYLAMINO-6-ETHYLAMINO-S-TRIAZINE
- 2-METHYLTHIO-4-ETHYLAMINO-6-ISOPROPYLAMINO-S-TRIAZINE
- N-ETHYL-N'-ISOPROPYL-6-METHYLTHIO-1,3,5-TRIAZINE-2,4-DIYLDIAMINE
- s-TRIAZINE, 2-ETHYLAMINO-4-ISOPROPYLAMINO-6-METHYLTHIO-