Benefin; CASRN 1861-40-1

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 Benefin

File First On-Line 03/31/1987

<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>
<td>yes</td>
<td>03/31/1987</td>
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<tr>
<td>Inhalation RfC (I.B.)</td>
<td>not evaluated</td>
<td></td>
</tr>
<tr>
<td>Carcinogenicity Assessment (II.)</td>
<td>not evaluated</td>
<td></td>
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I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Benefin  
CASRN — 1861-40-1  
Last Revised — 03/31/1987

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

<table>
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<tr>
<th>Critical Effect</th>
<th>Experimental Doses*</th>
<th>UF</th>
<th>MF</th>
<th>RfD</th>
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<tr>
<td>Depressed erythrocyte counts</td>
<td>NOAEL: 25 mg/kg/day</td>
<td>100</td>
<td>1</td>
<td>3E-1 mg/kg/day</td>
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<tr>
<td>Dog Chronic Oral Bioassay</td>
<td>LOAEL: 125 mg/kg/day</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Eli Lilly and Co., 1972</td>
<td></td>
<td></td>
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</table>

*Dose Conversion Factors & Assumptions: none

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


Results of a chronic oral bioassay in dogs (four animals/sex/dose) established a NOAEL of 25 mg/kg/day that was associated with a slight depression of erythrocyte counts with no reduction in blood hemoglobin concentrations or hematocrit, and a LOAEL of 125 mg/kg/day that was associated with increased relative liver weights and depressed blood hemoglobin concentrations and hematocrit. Additional studies support the choice of this effect level (i.e., 25 mg/kg/day) as the basis of the RfD. Teratogenic effects were not seen at doses up to 100 mg/kg/day in rabbits. Some reproductive problems were evident in rats at approximately 250 mg/kg/day, but not at 50 mg/kg/day.

The British Crop Protection Council (BCPC, 1977) reported NOELs for rats exposed orally to 1250 ppm/day (3 months) and greater than 500 ppm/day for dogs administered benefin in capsules. No experimental details were given.
I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — The 100-fold uncertainty factor represents 10-fold dose reductions for both the expected interhuman and interspecies variability to the toxicity of this chemical in lieu of specific data.

MF — None

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

Data regarding developmental toxicity are not available in the published literature.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Medium
RfD — Medium

Confidence in the chosen study is medium because, although three doses were tested and a good analysis was apparently performed, only four animals/sex/dose were used. The database rates a medium confidence; while not extensive, it is supportive of the chosen effect level. Medium confidence in the RfD follows.

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


The ADI in the 1984 Health and Environmental Effects Profile for Benefin received an Agency Review with the help of two external scientists.

Other EPA Documentation — None

Agency Work Group Review — 11/06/1985

Verification Date — 11/06/1985

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 Benefin 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 — Benefin
CASRN — 1861-40-1

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Benefin
CASRN — 1861-40-1

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 — Benefin
CASRN — 1861-40-1
VI.A. Oral RfD References


VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None
VII. Revision History

Substance Name — Benefin
CASRN — 1861-40-1

<table>
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<tr>
<th>Date</th>
<th>Section</th>
<th>Description</th>
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<td>12/03/2002</td>
<td>I.A.6.</td>
<td>Screening-Level Literature Review Findings message has been added.</td>
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VIII. Synonyms

Substance Name — Benefin
CASRN — 1861-40-1
Last Revised — 03/31/1987

- 1861-40-1
- BALAN
- BALFIN
- BANAFINE
- BENALAN
- BENEFEX
- Benefin
- BENFLURALIN
- BETHRODINE
- BINELL
- BLULAN
- BONALAN
- CARPIDOR
- EL-110
- EMBLEM
- L 54521
- N-BUTYL-2,6-DINITRO-N-ETHYL-4-TRIFLUOROMETHYLANILINE
- N-BUTYL-N-ETHYL-2,6-DINITRO-4-(TRIFLUOROMETHYL)BENZENAMINE
- N-BUTYL-N-ETHYL-alpha,alpha,alpha-TRIFLUORO-2,6-DINITRO-p-TOLUIDINE
- QUILAN
- p-TOLUIDINE, N-BUTYL-N-ETHYL-alpha,alpha,alpha-TRIFLUORO-2,6-DINITRO-
  alpha,alpha,alpha-TRIFLUORO-2,6-DINITRO-N,N-ETHYLIBUTYL-p-TOLUIDINE