Chlorobenzilate; CASRN 510-15-6

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 Chlorobenzilate

File First On-Line 12/01/1989

<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>12/01/1989</td>
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<tr>
<td>Inhalation RfC (I.B.)</td>
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<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 — Chlorobenzilate
CASRN — 510-15-6
Last Revised — 12/01/1989

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>
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</thead>
<tbody>
<tr>
<td>Decreased stool quantity, food consumption and body weight gains; hyperirritability</td>
<td>NOEL: 5 mg/kg/day (Maternal)</td>
<td>300</td>
<td>1</td>
<td>2E-2 mg/kg/day</td>
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<tr>
<td></td>
<td>LEL: 20 mg/kg/day (Maternal)</td>
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*R Conversion Factors: Actual dose tested

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


Three groups of pregnant New Zealand White rabbits (19/group) were treated with technical grade chlorobenzilate as a starch suspension containing Tween 80 at doses of 5, 20, or 80 mg chlorobenzilate/kg bw/day by gastric intubation on days 7 through 19 of gestation. The control group was intubated with an equivalent volume of 3% corn starch-Tween 80 suspension on the same days. The does were observed daily and were weighed on days 0, 7, 14, 19, 21, 25, and 29 of gestation. Feed consumption was measured daily from the time of insemination until necropsy.

On gestation day 29 the does and their fetuses were evaluated for maternal and developmental toxicity effects. No developmental effects were reported at any level [NOEL=80 mg/kg/day (HDT)]; although there was an increase in the incidence of "fused sternebrae" in the high-dose level fetuses. The maternal toxicity LEL was determined to be 20 mg/kg/day based on
significantly decreased feed consumption, decreased stools, decreased body weight gains, and hyperirritability. The maternal NOEL is therefore 5 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. An additional UF of 3 was used to account for the lack of an acceptable chronic oral toxicity study in a second species.

MF — None

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

Data Considered for Establishing the RfD

1) Teratology - rabbit: Principal study - see previous description; core grade minimum

2) 2-Year Feeding - dog: NOEL=500 ppm (12.5 mg/kg/day); LEL=5000/3000 ppm (125/75 mg/kg/day) (increased alkaline phosphatase, reduced serum protein levels, inappetance, reduced body weights and moderate to severe anemia; extramedullary hematopoiesis of the liver and spleen and erythroid hyperplasia of the bone marrow); After week 20 the 5000 ppm dose level was reduced to 3000 ppm; core grade minimum (Ciba-Geigy Corp., 1966)

3) 2-Generation Reproduction - rat: Systemic NOEL=30 mg/kg/day; Systemic LEL=100 mg/kg/day (HDT; decreased weight gain, increased liver weight, decreased spleen weight and hypoplasia of bone marrow for 8/30 F1 parent females); Reproductive NOEL=100 mg/kg/day (HDT); core grade guideline (Ciba-Geigy Corp., 1982)

4) Teratology - rat: Maternal NOEL=20 mg/kg/day; Maternal LEL=100 mg/kg/day (salivation, lethargy); Fetotoxic NOEL=100 mg/kg/day; Fetotoxic LEL=500 mg/kg/day (HDT; increased number of resorptions and post-implantation loss); Teratogenic NOEL=500 mg/kg/day (HDT); Teratogenic LEL=none; core grade minimum (Ciba-Geigy Corp., 1984b)

Data Gap(s): None
I.A.5. Confidence in the Oral RfD

- Study — Low
- Database — Medium
- RfD — Medium

The critical study is given a low confidence rating since the observed GI effects are somewhat equivocal. The supporting database is of good quality; thus, confidence in the database can be considered medium to high. Confidence in the RfD can also be considered medium to high.

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, March 1989; Pesticide Registration Files
- Agency Work Group Review — 05/20/1985, 05/17/1989
- Verification Date — 05/17/1989

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 Chlorobenzilate 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 — Chlorobenzilate
- CASRN — 510-15-6

Not available at this time.
II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Chlorobenzilate
CASRN — 510-15-6

Not available at this time.

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Chlorobenzilate
CASRN — 510-15-6

VI.A. Oral RfD References


VI.B. Inhalation RfC References

None
VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Chlorobenzilate
CASRN — 510-15-6

<table>
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<tr>
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<th>Description</th>
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VIII. Synonyms

Substance Name — Chlorobenzilate
CASRN — 510-15-6
Last Revised — 12/01/1989

- 510-15-6
- ACAR
- AKAR
- BENZENECETIC ACID, 4-CHLORO-ALPHA-(4-CHLOROPHENYL)-ALPHA-HYDROXY-, ETHYL ESTER
- BENZILAN
- BENZILIC ACID, 4,4'-DICHLOORO-, ETHYL ESTER
- BENZ-O-CHLOR
- CHLORBENZILAT
- CHLORBENZYLATE
- CHLOROBENZILATE
- CHLOROBENZYLATE
- COMPOUND 338
- 4,4'-DICHLOORBENZILSAEUREAETHYLESTER (GERMAN)
- 4,4'-DICHLOORBENZILATE
• 4,4’-DICHLOOROBENZILIC ACID ETHYL ESTER
• ENT 18,596
• ETHYL 4-CHLORO-ALPHA-(4-CHLOROPHENYL)-ALPHA-
  HYDROXYBENZENEACETATE
• ETHYL 4,4’-DICHLOOROBENZILATE
• ETHYL P,P’-DICHLOOROBENZILATE
• ETHYL 4,4’-DICHLOORODIPHENYL GLYCOLLATE
• ETHYL 4,4’-DICHLOOROPHENYL GLYCOLLATE
• ETHYLESTER KYSELINY 4,4-DICHLOBENZILOVE (CZECH)
• ETHYL ESTER OF 4,4’-DICHLOOROBENZILIC ACID
• ETHYL-2-HYDROXY-2,2-BIS(4-CHLOROPHENYL) ACETATE
• FOLBEX
• G 23992
• G 338
• GEIGY 338
• KOP-MITE
• NCI-C00408
• NCI-C60413
• RCRA WASTE NUMBER U038