Carbosulfan; CASRN 55285-14-8

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 Carbosulfan

File First On-Line 01/31/1987

<table>
<thead>
<tr>
<th>Category (section)</th>
<th>Assessment Available?</th>
<th>Last Revised</th>
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<tbody>
<tr>
<td>Oral RfD (I.A.)</td>
<td>yes</td>
<td>01/31/1987</td>
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<tr>
<td>Inhalation RfC (I.B.)</td>
<td>not evaluated</td>
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<tr>
<td>Carcinogenicity Assessment (II.)</td>
<td>not evaluated</td>
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I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Carbosulfan
CASRN — 55285-14-8
Last Revised — 01/31/1987

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>Decreased body weight</td>
<td>NOEL: 20 ppm diet (1 mg/kg/day)</td>
<td>100</td>
<td>1</td>
<td>1E-2 mg/kg/day</td>
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<tr>
<td>2-Year Rat Feeding Study</td>
<td>LEL: 500 ppm diet (25 mg/kg/day)</td>
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<td>FMC, 1982a</td>
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*Conversion Factors -- 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

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


Sixty male and 60 female Sprague-Dawley rats per dose were administered in their diet 0, 10, 20, 500, and 2500 ppm of carbosulfan for 24 months. Parameters evaluated were mortality, body weight, food consumption, water consumption, ophthalmoscopic examination, cholinesterase evaluation, hematology evaluation, clinical chemistry, urinalysis, necropsy evaluation, organ weights, and histopathologic evaluation of tissue. At 500 ppm, decreased body weight and food consumption, and increased incidence of toxic signs were observed. Brain, plasma and RBC cholinesterase inhibition was also observed at 500 ppm.

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

UF — Based on a chronic exposure study, an uncertainty factor of 100 was used to account for inter- and intraspecies differences.

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

Data Considered for Establishing the RfD:

1. 2-Year Feeding (oncogenic) - rat: Principal study - see previous description; core grade minimum
2. 3-Generation Reproduction - rat: NOEL=1 mg/kg/day; LEL=12.5 mg/kg/day (decreased pup weight and viability); core grade minimum (FMC Corp., 1982b)
3. 6-Month Feeding - dog: ChE NOEL=1.25 mg/kg/day; ChE LEL=12.5 mg/kg/day (plasma and RBC inhibition); core grade minimum (FMC Corp., 1980a)
4. Teratology - rat: Fetotoxic and Maternal NOEL=2 mg/kg/day; Fetotoxic and Maternal LEL=10 mg/kg/day (decreased body weight); core grade minimum (FMC Corp., 1980b)
5. Teratology - rabbit: Fetotoxic NOEL=5 mg/kg/day; LEL=10 mg/kg/day (decreased body weight); core grade minimum (FMC Corp., 1980c)

Other Data Reviewed:

1) 2-Year Feeding (oncogenic) - mice: ChE NOEL=10 ppm or 1.5 mg/kg/day; Plasma ChE LEL=20 ppm or 3 mg/kg/day; core grade minimum (FMC Corp., 1982c)

Data Gap(s): None

I.A.5. Confidence in the Oral RfD

Study — High
Database — High
RfD — High

The principal study appears to be of good quality and is given a high confidence rating. Additional studies are supportive and therefore, the data base is given a high confidence rating. High confidence in the RfD follows.

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

Pesticide Registration Files

Agency Work Group Review — 06/10/1986

Verification Date — 06/10/1986
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 Carbosulfan 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 — Carbosulfan
CASRN — 55285-14-8

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Carbosulfan
CASRN — 55285-14-8

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 — Carbosulfan
CASRN — 55285-14-8
VI.A. Oral RfD References


VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None
VII. Revision History

Substance Name — Carbosulfan
CASRN — 55285-14-8

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

Substance Name — Carbosulfan
CASRN — 55285-14-8
Last Revised — 01/31/1987

- 55285-14-8
- ADVANTAGE
- CARBAMIC ACID, ((DIBUTYLAMINO)THIO)METHYL-, 2,2-DIMETHYL-2,3-DIHYDRO-7- BENZOFURANYL ESTER
- Carbosulfan
- ((DIBUTYLAMINO)THIO)METHYL-CARBAMIC ACID, 2,2-DIMETHYL-2,3-DIHYDRO-7- BENZOFURANYL ESTER
- 2,3-DIHYDRO-2,2-DIMETHYL-7-BENZOFURANYL(DI-n-BUTYLAMINOSULFENYL)METHYLCARBAMATE
- 2,3-DIHYDRO-2,2-DIMETHYL-7-BENZOFURANYL((DIBUTYLAMINO)THIO)METHYL CARBAMATE
- FMC 35001
- MARSHAL