Sethoxydim; CASRN 74051-80-2

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 Sethoxydim

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>11/01/1989</td>
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<tr>
<td>Inhalation RfC (I.B.)</td>
<td>not evaluated</td>
<td></td>
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<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 — Sethoxydim
CASRN — 74051-80-2
Last Revised — 11/01/1989

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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<tbody>
<tr>
<td>Mild anemia in males</td>
<td>NOEL: 8.86/9.41 mg/kg/day (Male/Female)</td>
<td>100</td>
<td>1</td>
<td>9E-2 mg/kg/day</td>
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<tr>
<td>1-Year Dog Study Oral Exposure (diet)</td>
<td>LEL: 17.5/19.9 mg/kg/day (Male/Female)</td>
<td></td>
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<tr>
<td>BASF Corporation, 1984</td>
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*Conversion Factors -- Actual dose tested.

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


Groups of 6 male and 6 female beagle dogs were orally dosed with NP-55 (96.86% pure technical sethoxydim) in their feed at concentrations of 0 (vehicle control), 300, 600, and 3600 ppm. The measured male/female doses were 0, 8.86/9.41, 17.5/19.9, and 110/129 mg/kg/day. The dogs were observed twice daily for clinical signs and weekly for body weight changes and food consumption. Water consumption was measured during weeks 12, 25, 39, and 51. Ophthalmologic examinations were conducted pretest, and at 6 and 12 months. Urine and jugular blood were collected from fasted dogs at study initiation, and at 1, 2, 3, 4, 5, 6, and 12 months. All dogs were examined grossly and their tissues were evaluated histopathologically.

No dogs died during this study, and no-compound related neoplastic lesions were found. The target organs were bone marrow and the liver. The NOEL for this study is 300 ppm (8.86/9.41 mg/kg/day, M/F). The LEL is 600 ppm (17.5/19.9 mg/kg/day, M/F) based upon mild anemia observed in males.
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.

MF — None

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

Data Considered for Establishing the RfD

1) 1-Year Feeding - dog: Principal study - see previous description;

2) 2-Year Feeding (oncogenic) - rat: NOEL=360 ppm (18 mg/kg/day) (HDT); LEL=None; core grade guideline (BASF, 1981a)

3) 2-Generation Reproduction - rat: Systemic NOEL=360 ppm (18 mg/kg/day); Systemic LEL=1080 ppm (162 mg/kg/day) (decreased body weight gain, increased male thyroid and female adrenal weights); Reproductive NOEL=1080/3240 ppm (54/162 mg/kg/day); Reproductive LEL=None; core grade guideline (BASF, 1980a)

4) Teratology - rat: Maternal NOEL=40 mg/kg/day; Maternal LEL=100 mg/kg/day (significantly reduced adrenal weights); Developmental NOEL=250 mg/kg/day (HDT); Developmental LEL=None; core grade guideline (BASF, 1980b)

5) Teratology - rabbit: Maternal NOEL=160 mg/kg/day; Maternal LEL=480 mg/kg/day (severe weight loss, 5/16 deaths, 6/16 abortions, reduction in number of litters and viable fetuses); Developmental NOEL=160 mg/kg/day; Developmental LEL=480 mg/kg/day (increased number of random effects including skeletal and visceral abnormalities, reduced fetal weight and severe maternal toxicity); core grade guideline (BASF, 1980c)

Other Data Reviewed:

1) 2-Year Feeding (oncogenic) - mouse: Systemic NOEL=120 ppm (18 mg/kg/day); Systemic LEL=360 ppm (54 mg/kg/day) (non-neoplastic liver lesions); core grade guideline (BASF, 1981b)

2) 6-Month Feeding - dog: NOEL=600 ppm (20 mg/kg/day); LEL=6000 ppm (177/223 mg/kg/day) (liver effects and nonspecific anemia); core grade guideline (Nippon Soda Co., Ltd., 1981)
Data Gap(s): None

I.A.5. Confidence in the Oral RfD

Study — High
Database — High
RfD — High

The critical study is of good quality and is given a high confidence rating. Additional studies are also of good quality; therefore the database 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


Verification Date — 06/15/1989

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 sethoxydim 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 — Sethoxydim
CASRN — 74051-80-2

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

Substance Name — Sethoxydim
CASRN — 74051-80-2

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 — Sethoxydim
CASRN — 74051-80-2

VI.A. Oral RfD References


VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Sethoxydim
CASRN — 74051-80-2

<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Description</th>
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<tr>
<td>07/01/1989</td>
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<td>11/01/1989</td>
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<td>Oral RfD summary replaced; RfD changed</td>
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<td>10/28/2003</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 — Sethoxydim
CASRN — 74051-80-2
Last Revised — 03/31/1987

- 74051-80-2
- BAS 9052
- 2-CYCLOHEXEN-1-ONE, 2-(1-(ETHOXYIMINO)BUTYL)-5-(2-(ETHYLTHIO)PROPYL)-3-HYDROXY-
  CYETHOXYDIM
- 2-(1-(ETHOXYIMINO)BUTYL)-5-(2-(ETHYLTHIO)PROPYL)-3-HYDROXY-2-
  CYCLOHEXEN-1-ONE
- NABU
- NP 55
- POAST
- Sethoxydim