6-15-89

Sethoxydim RfD-1

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name: Sethoxydim
CASRN: 74051-80-2

The Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. 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 Oral RfD Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of compounds which 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 the Carcinogenicity Assessment Section of this file when a review of that evaluation is completed.

RfD ASSESSMENT SUMMARY TABLE

Crit. Dose: 8.86 mg/kg-day [Study 1 NOAEL]
UF: 100 MF: 1 RfD: 9E-2 mg/kg-day Confidence: High

Crit Effect: (1) Mild anemia in males

	NOAEL (Study 1)	LOAEL (Study 1)
Reported	8.86/9.41 mg/kg-day (Male/Female)	17.5/19.9 mg/kg-day (Male/Female)
ADJ	8.86 mg/kg-day	17.5 mg/kg-day
Study Type	1-Year Dog Study Oral Exposure (diet)	1-Year Dog Study Oral Exposure (diet)
Reference	BASF Corporation, 1984	BASF Corporation, 1984

1) BASF Corporation, 1984
1-Year Dog Study Oral Exposure (diet)

Critical Effect: Mild anemia in males

Defined Dose Levels:
NOAEL= 8.86/9.41 mg/kg-day (Male/Female)
NOAEL(ADJ)= 8.86 mg/kg-day
LOAEL= 17.5/19.9 mg/kg-day (Male/Female)
LOAEL(ADJ)= 17.5 mg/kg-day

Conversion Factors: Actual dose tested

DISCUSSION OF PRINCIPAL AND SUPPORTING STUDIES

BASF Corporation Chemicals Division. 1984. MRID No. 00152669. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

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

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control), 300, 600, and 3600 ppm. The measued 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.

UNCERTAINTY AND MODIFYING FACTORS

UNCERTAINTY FACTORS:

An uncertainty factor of 100 was used to account for the inter- and intraspecies differences.

ADDITIONAL COMMENTS / STUDIES

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)

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Data Gap(s): None

CONFIDENCE IN THE RfD

Study: High Data Base: 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 data base is given a high confidence rating. High confidence in the RfD follows.

EPA DOCUMENTATION AND REVIEW

Source Document: This assessment is not presented in any existing U.S. EPA document.

Other EPA Documention: Pesticide Registration Files

Agency Work Group Review: 09/02/86, 10/28/86, 06/15/89

Verification Date: 06/15/89

EPA CONTACTS

William Burnam / OPP -- (703)305-7491

George Ghali / OPP -- (703)305-7490

BIBLIOGRAPHY

BASF Corporation Chemicals Division. 1984. MRID No. 00152669. Available from EPA. Write to FOI, EPA, Washington DC 20460.

BASF Wyandotte Corporation. 1980a. MRID No. 00045867. Available from EPA. Write to FOI, EPA, Washington DC 20460.

BASF Wyandotte Corporation. 1980b. MRID No. 00045863. Available from EPA. Write to FOI, EPA, Washington DC 20460.

BASF Wyandotte Corporation. 1980c. MRID No. 00045864. Available from EPA. Write to FOI, EPA, Washington DC 20460.

BASF Wyandotte Corporation. 1981a. MRID No. 00100526. Available from EPA. Write to FOI, EPA, Washington DC 20460.

BASF Wyandotte Corporation. 1981b. MRID No. 00100527. Available from EPA. Write to FOI, EPA, Washington DC 20460.

Nippon Soda Company, Ltd. 1981. Accession No. 099996. Available from EPA. Write to FOI, EPA, Washington DC 20460.

REVISION HISTORY

03/88 RfD Confid: Confidence levels revised
07/89 RfD Data: Withdrawn; new Oral RfD verified (in preparation)

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

11/89 RfD Data: Oral RfD summary replaced; RfD changed