9-16-87

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name: Pendimethalin
CASRN: 40487-42-1
Primary Synonym: Prowl

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: 12.5 mg/kg-day [Study 1 NOAEL]
UF: 300 MF: 1 RfD: 4E-2 mg/kg-day Confidence: Medium

Crit Effect: (1) Increase in serum alkaline phosphatase and liver weight, and hepatic lesions

	NOAEL (Study 1)	LOAEL (Study 1)
Reported	12.5 mg/kg-day	50 mg/kg-day
ADJ	12.5 mg/kg-day	50 mg/kg-day
Study Type	2-Year Dog Feeding Study	2-Year Dog Feeding Study
Reference	American Cyanamid, 1979	American Cyanamid, 1979

1) American Cyanamid, 1979
2-Year Dog Feeding Study

Critical Effect: Increase in serum alkaline phosphatase and liver weight, and hepatic lesions

Defined Dose Levels:
NOAEL= 12.5 mg/kg-day
NOAEL(ADJ)= 12.5 mg/kg-day
LOAEL= 50 mg/kg-day
LOAEL(ADJ)= 50 mg/kg-day

Conversion Factors: none

DISCUSSION OF PRINCIPAL AND SUPPORTING STUDIES

American Cyanamid Co. 1979. MRID No. 00058657. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

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Purebred beagle dogs, 4/sex/dose, were fed pendimethalin 7 days a week by gelatin capsule at 0, 12.5, 50, and 200 mg/kg/day. Clinical chemistry findings were considered within normal limits for all dose levels however, serum alkaline phosphatase (SAP) was increased at the mid- and high-dose levels. Liver weights were increased and the liver showed lesions consisting of inflammation and hemosiderosis at the mid- and high-dose levels. The NOEL and LEL for systemic toxicity are 12.5 and 50 mg/kg/day, respectively, based on hepatic lesions and an increase in SAP and liver weights.

UNCERTAINTY AND MODIFYING FACTORS

UNCERTAINTY FACTORS:

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 long term study in a second species. A factor of 3 was chosen rather than 10 since the studies at hand, although of insufficient quality, indicate that the dog is the more sensitive species, and since there is no significant difference in subchronic and chronic effects for this chemical.

ADDITIONAL COMMENTS / STUDIES

Data Considered for Establishing the RfD:

1) 2-Year Feeding - dog: Principal study - see previous description; core grade minimum (American Cyanamid Co., 1979a)

2) 3-Generation Reproduction - rat: Reproductive NOEL=500 ppm (25 mg/kg/day); Reproductive LEL=5000 ppm (250 mg/kg/day) (HDT; reduced litter size, survival index, and pup weight); core grade minimum (American Cyanamid Co., 1974a)

3) Teratology - rat: Fetotoxic and Teratogenic NOEL=500 mg/kg/day (HDT); core grade guideline (American Cyanamid Co., 1979b)

4) Teratology - rabbit: NOEL=60 mg/kg/day (HDT); core grade minimum (American Cyanamid Co., 1982)

Other Data Reviewed:

1) 90-Day Feeding - rat: NOEL=500 ppm (25 mg/kg/day); LEL=5000 ppm (250 mg/kg/day) (decrease in hematocint and hemoglobin in males, decreased body weight and food consumption, hypertrophy of the liver accompanied by increased liver weights); core grade guideline (American Cyanamid Co., 1974b)

2) 90-Day Feeding - dog: NOEL=2500 ppm (62.5 mg/kg/day) (by gavage); no core grade (American Cyanamid Co., 1973)

Data Gap(s): Chronic Rat Feeding Study

CONFIDENCE IN THE RfD

Study: Medium Data Base: Medium RfD: Medium

The critical study appears to be of good quality and is given a medium

confidence rating. Since the data base on chronic toxcity is supportive but incomplete, the data base is given a medium confidence rating. Medium 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 Standard, September 1984; Pesticide Registration Files

Agency Work Group Review: 08/19/86, 09/16/87

Verification Date: 09/16/87

EPA CONTACTS

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American Cyanamid Company. 1974a. MRID No. 00026671, 00059470, 00106762. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1974b. MRID No. 00026667, 00026668, 00040302. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1979a. MRID No. 00058657. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1979b. MRID No. 00025752. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

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REVISION HISTORY

02/91 RfD Data: Text edited