9-1-88

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name: Terbutryn
CASRN: 886-50-0

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: 0.1 mg/kg-day [Study 1 NOAEL(adj)]
UF: 100 MF: 1 RfD: 1E-3 mg/kg-day Confidence: High

Crit Effect: (1) Hematologic effects in females

	NOAEL (Study 1)	LOAEL (Study 1)
Reported	2 ppm	300 ppm
ADJ	0.1 mg/kg-day	15 mg/kg-day
Study Type	2-Year Rat Feeding Study	2-Year Rat Feeding Study
Reference	Ciba-Geigy, 1980a	Ciba-Geigy, 1980a

1) Ciba-Geigy, 1980a
2-Year Rat Feeding Study

Critical Effect: Hematologic effects in females

Defined Dose Levels:
NOAEL= 2 ppm
NOAEL(ADJ)= 0.1 mg/kg-day
LOAEL= 300 ppm
LOAEL(ADJ)= 15 mg/kg-day

Conversion Factors: 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

DISCUSSION OF PRINCIPAL AND SUPPORTING STUDIES

Ciba-Geigy Corporation. 1980a. MRID No. 00035923. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Two hundred sixty male and 260 female weanling Charles River CD rats were randomly distributed into the following groups: 0, (70 animals/sex), 2 (60

animals/sex), 300 (60 animals/sex) and 3000 ppm (70 animals/sex) (0, 0.1, 15, and 150 mg/kg/day) and administered terbutryn in their diets for 2 years. Based upon a statistical reevaluation of the hematologic data from this study, a NOEL for systemic effects can be set at 2 ppm. The LEL is 300 ppm based upon a statistically significant and dose-related decrease in hemoglobin and erythrocytes in female rats at 18 months. This parameter was not measured for the mid-dose group at term. At the HDT (3000 ppm) there was also a statistically significant decrease in hematocrit in females at both 18 and 24 months.

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) 2-Year Feeding (oncogenic) - rat: Principal study - see previous description; core grade minimum

2) 6-Month Feeding - dog: NOEL=10 mg/kg/day; LEL=25 mg/kg/day (mucosal thickening of various segments of the small intestine and submucosal lymphoid hyperplasia in the stomach); core grade minimum (Ciba-Geigy Corp., 1980b)

3) 3-Generation Reproduction - rat: NOEL=15 mg/kg/day; LEL=150 mg/kg/day (decreased body weight gain and decreased fertility indices in males and females); core grade minimum (Ciba-Geigy Corp., 1980c)

4) Teratology - rat: Maternal NOEL=50 mg/kg/day; Maternal LEL=500 mg/kg/day (reduced body weight); Developmental NOEL=50 mg/kg/day; Developmental LEL=500 mg/kg/day (weight decrease, reduced ossification - front and rear paws); core grade minimum (Ciba-Geigy Corp., 1985a)

5) Teratology - rabbit: Maternal NOEL=10 mg/kg/day; Maternal LEL=50 mg/kg/day (body weight loss); Developmental NOEL=50 mg/kg/day; Developmental LEL=75 mg/kg/day (reduced ossification of sternebrae); core grade guideline (Ciba-Geigy Corp., 1985b)

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 supportive; therefore, the data base is given a high confidence rating. High confidence in the RfD follows.

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

EPA DOCUMENTATION AND REVIEW

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

Other EPA Documention: Pesticide Registration Standard, July 1986; Pesticide Registration Files

Agency Work Group Review: 07/15/87, 08/13/87, 07/20/88

Verification Date: 07/20/88

EPA CONTACTS

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

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

BIBLIOGRAPHY

Ciba-Geigy Corporation. 1980a. MRID No. 00035923. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1980b. MRID No. 00029152. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1980c. MRID No. 00035659. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1985a. MRID No. 00152764. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1985b. MRID No. 00152763. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

REVISION HISTORY

09/88 RfD Data: Oral RfD summary on-line