10-1-90

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name: Propazine
CASRN: 139-40-2

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: 5 mg/kg-day [Study 1 NOAEL(adj)]
UF: 300 MF: 1 RfD: 2E-2 mg/kg-day Confidence: Medium

Crit Effect: (1) Decrease in body weight

	NOAEL (Study 1)	LOAEL (Study 1)
Reported	100 ppm (diet)	1000 ppm (diet)
ADJ	5 mg/kg-day	50 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: Decrease in body weight

Defined Dose Levels:
NOAEL= 100 ppm (diet)
NOAEL(ADJ)= 5 mg/kg-day
LOAEL= 1000 ppm (diet)
LOAEL(ADJ)= 50 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. 00041408, 00076955, 00087893. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Two hundred and sixty males and 260 female CD rats were selected randomly and given 0, 3, 100 or 1000 ppm of propazine in their diets for 2 years. Seventy

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

animals of each sex were placed in the control and high dose group. Sixty animals of each sex were placed in the low and mid-dose groups. At 1000 ppm there was a significant decrease in body weight in both sexes. There was a significant increase in mammary tumors in females at 1000 ppm. The NOEL for systemic effects was 100 ppm (5 mg/kg/day).

An RfD based on the subchronic dog NOEL of 5 mg/kg/day and a 1000 UF, to account for inter- and intraspecies differences and a subchronic-to-chronic extrapolation, would yield a value similar to the RfD.

UNCERTAINTY AND MODIFYING FACTORS

UNCERTAINTY FACTORS:

An uncertainty factor of 100 is used to account for the inter- and intraspecies differences. An additional UF is used to account for the fact that the data base on chronic toxicity lacks an adequate second mammalian bioassay (that is, a chronic feeding study in the dog may yield a more sensitive toxicological endpoint). However, since the 90-day studies in rats and dogs do not show an order of magnitude species difference, an additional 3-fold UF is considered appropriate.

ADDITIONAL COMMENTS / STUDIES

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=5 mg/kg/day; LEL=50 mg/kg/day (reduced mean pup body weight); core grade minimum (Ciba-Geigy, 1979)

3) Teratology - Rat: Fetotoxic NOEL=100 mg/kg/day; Fetotoxic LEL=300 mg/kg/day; Maternal Toxic NOEL=100 mg/kg/day; Maternal Toxic LEL=300 mg/kg/day; core grade supplementary (Ciba-Geigy, 1976)

4) 90-Day Feeding - Dog: NOEL=200 ppm (5 mg/kg/day); LEL=1000 ppm (HDT) (25 mg/kg/day) (decreased body weight); no core grade (Ciba-Geigy, 1967)

Other Data Reviewed:

1) 2-Year Feeding (oncogenic) - Mouse: Systemic NOEL=15 mg/kg/day; Systemic LEL=450 mg/kg/day; (increased focal myocardial fibrosis and focal myocardial degeneration); core grade minimum (Ciba-Geigy, 1980b)

Data Gap(s): Chronic Dog Feeding Study; Rat Teratology Study; Rabbit Teratology Study

CONFIDENCE IN THE RfD

Study: Medium Data Base: Medium RfD: Medium

The critical study appears to be of fair quality and is given a medium confidence rating. Additional studies are supportive, but because there are data gaps, 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 Files

Agency Work Group Review: 08/19/86, 09/29/86, 05/20/87

Verification Date: 05/20/87

EPA CONTACTS

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

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

BIBLIOGRAPHY

Ciba-Geigy Corporation. 1980a. MRID No. 00041408, 00076955, 00087893. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1979. MRID No. 00041409. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1976. MRID No. 00087879. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1967. MRID No. 0011680. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1980b. MRID No. 00044335. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

REVISION HISTORY

08/87 RfD Data: UF reevaluated - RfD changed
10/90 RfD Add Com: Citations added