6-27-86

REFERENCE DOSES (RFDs) FOR ORAL EXPOSURE

Chemical: Propazine

CAS #: 139-40-2
Caswell #: 184

Carcinogenicity: Preliminary evidence of oncogenicity in female rats (increased incidence of mammory tumors) is under review.

Systemic Toxicity: See below.

Preparation Date: 6/27/86

Endpoint	Experimental Doses	UF	MF	RfD
IRDC (1980) 2-Year Rat Feeding/ Oncogenicity Study	100 ppm (5 mg/kg/day) Systemic NOEL	100	10	0.005 mg/kg/day
decrease in body weight	1000 ppm (50 mg/kg/day) Systemic LEL			

Conversion factor (rat): 1 ppm = 0.05 mg/kg/day

Endpoint and Experimental Doses:

2-Year Rat Feeding/Oncogenicity Study
IRDC
Report No. 382-007; April 28, 1980

Two hundred and sixty males and 260 female CD rats were selected randomly and given 0, 3, 100, and 1000 ppm of propazine in their diets for 2 years. At 1000 ppm there was a significant decrease in body weight in both sexes. There was an significant increase in mammary tumors in females at 1000 ppm. The NOEL for Systemic effects is 100 ppm (5 mg/kg/day).

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Uncertainty Factors (UFs):

Based on a chronic exposure study, an uncertainty factor of 100 was used to account for the inter- and intraspecies differences.

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Modifying Factors (MFs):

An additional MF of 10 was used to account for the fact that the data base on chronic toxicity is incomplete and a chronic feeding study in the dog may yield a more sensitive toxicological endpoint.

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Additional Comments:

Data Considered for Establishing the RfD

1) 2-Year Feeding/Oncogenic - Rat (NOEL = 100 ppm (5 mg/kg/day), LEL = 1000 ppm (50 mg/kg/day)(decreased body weight); Oncogenic NOEL = 100 ppm, Oncogenic LEL = 1000 ppm (increase in mammary tumors); minimum)

2) 3-Generation Reproduction - Rat (NOEL = 5 mg/kg, LEL = 50 mg/kg; reduced mean pup body weight; minimum)

3) Teratology - Rat (Fetotoxic NOEL = 100 mg/kg, Fetotoxic LEL = 300 mg/kg; Maternal toxic NOEL = 100 mg/kg, Maternal toxic LEL = 300 mg/kg; supplementary)

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)

Data Gap(s)

1) Chronic Dog Feeding Study
2) Rat Teratology Study
3) Rabbit Teratology Study

Other Data Considered

1) 2-Year Feeding/Oncogenic - Mice (NOEL = 15 mg/kg; LEL = 450 mg/kg; increased focal myocardial fibrosis and focal myocardial degeneration; negative for oncogenicity up to 450 mg/kg; minimum)

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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 since there are data gaps existing the RfD is given a medium confidence rating.

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Documentation of RfD and Review:

Registration Files

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Agency RfD Review:

First Review: 8/19/86
Second Review: 9/29/86
Verification Date: 8/29/86

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