OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

125601 3

REFERENCE DOSES (RFDs) FOR ORAL EXPOSURE

Chemical: Paclobutrazol

CAS #: 76738-62-0
Caswell #: 628C

Carcinogenicity: No studies available

Systemic Toxicity: See below.

Preparation Date: 7/21/86

| Endpoint | Experimental Doses | UF | MF | RfD |
|---|---|---|---|---|
| Imperial Chemical Industries PLC, Central Tox. Lab. 90-Day Rat Feeding Study | 250 ppm (12.5 mg/kg/day) NOEL<br>1250 ppm (62.5 mg/kg/day) LEL | 1000 | — | 0.013 mg/kg/day |

At 1250 ppm liver weights were elevated in females along with serum cholesterol, hepatic aminopyrine N-demethylase activity, and alanine transaminase levels

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

Endpoint and Experimental Doses:

Litchfield, M.H., P.B. Banham, et. al.
90-Day Rat Feeding Study
Imperial Chemical Industries PLC, Central Tox. Lab.
Report no. CTL/P/760; July 16, 1983

Four groups of Wistar rats (20/sex/dose level) were fed diets containing 0, 50, 250, or 1250 ppm of Paclobutrazol for 90 days. At 1250 ppm liver weights were elevated in females along with serum cholesterol, hepatic aminopyrine N-demethylase activity, and alanine transaminase levels. The lowest dose tested was 50 ppm. No effects were seen in male rats.

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Uncertainty Factors (UFs):

Based on a subchronic exposure study, an uncertainty factor of 1000 was used to account for inter- and intraspecies differences and for the insufficient duration of the study to fully assess chronic effects.

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Modifying Factors (MFs):

None

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Additional Comments: None

Data Considered for Establishing the RfD

1) 90-Day Feeding - Rat NOEL = 250 ppm (12.5 mg/kg/day), LEL = 1250 ppm (62.5 mg/kg/day) (At 1250 ppm liver weights were elevated in females along with serum cholesterol, hepatic aminopyrene N-demethylase activity, and alanine transaminase levels. 50 ppm was the lowest dose tested. No effects in males); core grade minimum

2) 1-Year Feeding - Dog NOEL = 15 mg/kg/day, LEL = 75 mg/kg/day (increased liver weight, increased serum alkaline phosphatase and triglyceride levels, increased hepatic aminopyrine N-demethylase activity, and enlarged hepatocytes); core grade minimum

3) 6-Week Oral Dosing - Dog NOEL = 15 mg/kg/day (lowest dose tested), LEL = 75 mg/kg/day. (At doses of 75 and 225 mg/kg dogs had increased liver weights and serum alkaline phosphatase levels. Only one male and one female dog was tested at each dose); core grade supplementary

4) Teratology - Rat NOEL (Maternal toxicity) = 40 mg/kg/day (lowest dose tested), LEL = 100 mg/kg/day ( 250 mg/kg/day (highest dose tested) caused mortality (5/24), liver enlargement, and pallor of the liver. 100 mg/kg/day caused slight decrease in bodyweight gain and food utilization efficiency. No NOEL established for Fetotoxicity (increased incidence of delayed ossification in fetuses). The 250 mg/kg/day dose also induced cleft palate in 3 fetuses from 2 litters.); core grade supplementary.

5) Teratology - Rat NOEL (Maternal toxicity) > 100 mg/kg/day (highest dose tested), NOEL (Fetotoxicity) = 10 mg/kg/day, LEL = 40 mg/kg/day (hydronephrosis, hydroureter, delayed ossification, minor skeletal defects); core grade minimum

6) Teratology - Rabbit NOEL (Maternal toxicity) = 25 mg/kg/day, LEL = 75 mg/kg/day (decreased body weight gain) NOEL (Fetotoxicity) > 125 mg/kg (highest dose tested) (Low fertility with only the mid and low dose groups having the minimal number of animals required); core grade supplementary

Data Gap(s)

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

Other Data Considered

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Confidence in the RfD:

Study: Medium Data Base: Medium RfD: Medium

The critical study is of good quality and is given a medium confidence rating. Additional studies are supportive but the data base on chronic toxicity is incomplete and therefore, 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: 9/02/86
Second Review:
Verification Date: 9/02/86

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