REFERENCE DOSES (RFDs) FOR ORAL EXPOSURE

Chemical: Oryzalin

CAS #: 19044-88-3
Caswell #: 623A

Carcinogenicity: Evidence of oncogenic effects in rats, no evidence in mice
Classified as Category C oncogen

Systemic Toxicity: See below.

Preparation Date: 3/6/86

Endpoint	Experimental Doses	UF	MF	RfD
Carter et al. (1980)	12.50 mg/kg/day (NOEL)	1000	-	0.013 mg/kg/day
3-Generation Reproduction Rat Study				
Depressed growth	3.7 mg/kg/day (LEL)			

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

Endpoint and Experimental Doses:

J.L. Carter et al. (1980)
Three Generation Reproduction Rat Study
Toxicology Division, Lilly Research Laboratories;
Studies R-1226, R-327, and R-647

Groups of 25 males and 25 females, 5 week-old Fischer 344 rats, received Oryzalin in the diet at 0, 250, 750, and 2250 ppm for 59, 63, and 73 days during the respective growth phases of F_0, F_1, and F_2 parental generations. Rats were mated and females allowed to deliver and raise offspring to 21 days of age. F_3 progeny were sacraficed as weanlings. F_0 and F_1 parents were sacraficed after begining of growth phase of their offspring. The F_2 parents were sacraficed after the F_3 progeny were killed. Oryzalin did not affect reproductive indices, litter size, length of gestation, or sex distribution of progeny. At 750 ppm there was growth suppression.

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Uncertainty Factors (UFs):

An uncertainty factor of 1000 has been used to account for the intra and inter species difference in extrapolation from the rat to the human, and to account for the fact that the NOEL in the reproduction study is not fully supported by chronic studies.

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Modifying Factors (MFs):

None

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Additional Comments:

Data Considered for Establishing the RfD

1) Teratology - Rabbit (Maternal and Fetotoxic NOEL=25 mg/kg; Maternal and Fetotoxic LEL=55 mg/kg, decreased litter size, increased resorptions, decreased maternal food consumption and weight gain; guideline)

2) Teratology - Rat (Teratogenic and Maternal NOEL >225 mg/kg (HDT); minimum)

3) 3-Generation Reproduction - Rat (Reproduction NOEL > 112.50 mg/kg (HDT); Fetotoxic NOEL=12.50 mg/kg; Fetotoxic LEL=37.50 mg/kg, depressed growth; minimum)

4) 3-Month Feeding - Dog (NOEL=18.75 mg/kg; LEL=56.25 mg/kg, reduced Hb, Hct, and RBC; increased BUN, alkaline phosphatase, blood sugar and SGPT; hyperplastic bone marrow, splenic hematopoiesis, anemia, and hepatic changes; no core grade)

5) 2 Year Feeding/Oncogenic - Rat (NOEL=15 mg/kg; LEL=45 mg/kg, increased leukocyte counts, BUN, liver and kidney weight; a positive oncogen; minimum)

Data Gap(s)

1) Chronic Dog Feeding Study

Other Data Considered

1) 2-Year Feeding/Oncogenic - Mice (Oncogenic NOEL >3650 ppm or 547.5 mg/kg (HDT); Systemic NOEL=75 mg/kg; LEL=202.5 mg/kg, decreased uterus and ovary weight; minimum)

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Confidence in the RfD:

Study: Medium Data Base: Medium RfD: Medium

The critical study is of moderate quality and therefore is given medium confidence. Additional studies are moderately supportive; however there is a chronic dog study as a data gap and the RfD is given a medium confidence.

Documentation of RfD and Review:

Registration Standard to be issued April-May 1986 (Science Chapter completed)

Agency RfD Review:

First Review: 3/25/86
Second Review:
Verification Date: 3/25/86

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