REFERENCE DOSES (RFDs) FOR ORAL EXPOSURE

Verified 08 10.

Chemical: Sethoxydim (Poast®)

CAS #: Not available
Caswell #: 72A

Carcinogenicity: No evidence of carcinogenicity in two adequate animal tests (rat and mouse).

Systemic Toxicity: See below.

Preparation Date: 8/18/86

Endpoint	Experimental Doses	UF	MF	RfD
IRDC (1981) 6-Month Dog Feeding Study	60 ppm (2 mg/kg/day) Systemic NOEL 600 ppm (20 mg/kg/day) Systemic LEL	100	—	0.02 mg/kg/day

Kidney and liver lesions

Conversion factor (dog): 1 ppm = 0.025 mg/kg/day

Endpoint and Experimental Doses:

Six-Month Dog Feeding Study;
International Research and Development Corporation
Report 449-004; March 9, 1981;

Groups of 6 male and 6 female beagles (4.5 months old) were fed diets containing 0 (controls), 2.0, 20.0, and 200.0 mg/kg/day (0, 60, 600, and 6000 ppm, respectively) of technical sethoxydim calculated on the basis of diet analyses and food consumption). They were presumably fed the formulated diet daily. They were observed twice daily for clinical signs, and weekly for body weights and food consumption. Eyes were examined ophthalmologically prior to dosing, and at 3 and 6 months. Blood was drawn and evaluated monthly, and urinalysis was performed at 2, 4, and 6 months. A phenosulfonphthalein (PSP) clearance test was performed prior to dosing and at 6 months. A bromsulphalein (BSP) serum retention test was performed prior to dosing and at 3 and 6 months. All dogs were examined grossly and histopathologically, and their organs were weighed. The defined values (revised from the original DER) are as follows:

NOEL = 2.0 mg/kg/day (60 ppm)
LEL = 20.0 mg/kg/day (600 ppm) [PSP clearance decreases (decreased kidney output)]

This study appeared to be well performed, but it did not resolve why the beagles in a Hazleton study were so profoundly affected by kidney toxicity at doses < 3.0 mg/kg/day.

Uncertainty Factors (UFs):

An uncertainty factor of 100 was used to account for the inter- and intraspecies differences.

Modifying Factors (MFs):

None

Additional Comments:

Data Considered for Establishing the RfD

1) 2-Year Feeding/Oncogenic - Rat Systemic and Oncogenic NOEL = 18 mg/kg/day (HDT); core grade guideline

2) 6-Month Feeding - Dog NOEL = 2.0 mg/kg/day; LEL = 20.0 mg/kg/day (possible pathogenic changes in the kidney). core grade guideline [Note: The NOEL and LEL are decreased from what is presented in the original review. A 1-Year Feeding Study in Dogs was not performed, since prevailing requirements (prior to October, 1982) only required a 6-month study. ~~Because the issue of nephrotoxicity remains unresolved, a one-year dog study is now required. The performing laboratory must be alerted to the nephrotoxic potential of [illegible]~~

6-Month Feeding - Dog NOEL < 3.0 mg/kg/day (LDT - cystitis and/or urinary calculi, blood urine, decreased PSP clearance and A/G levels, increased thyroid weights); core grade supplementary [Note: This study was repeated (above) because it was poorly performed and because of the discovery of nephrotoxicity at doses < 3.0 mg/kg/day.]

3) 2-Generation Reproduction - Rat Systemic NOEL = 18 mg/kg/day; no reproductive effects were seen at doses as high as 162 mg/kg/day; core grade guideline

4) Teratogenicity - Rat Maternal NOEL = 40 mg/kg/day; Maternal LEL = 150 mg/kg/day (significantly reduced adrenal weights); Teratogenic NOEL >250 mg/kg/day (HDT); core grade guideline

5) Teratogenicity - Rabbit Maternal NOEL = 160 mg/kg/day; Maternal LEL = 480 mg/kg/day (severe weight loss, 5/16 deaths, 6/16 abortions, reduction in number of litters, and viable fetuses); Teratogenic NOEL = 160 mg/kg/day; core grade guideline

A 1 year study is not required since this study was well performed.

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Data Gap(s)

Differences in nephrotoxicity results of the two 6-Month dog studies remain unresolved. The core guideline study is considered acceptable.

Other Data Considered

1) 2-Year Feeding/Oncogenic - Mouse Systemic and Oncogenic NOEL = 18 mg/kg/day; LEL = 54 mg/kg (non-neoplastic liver lesions); core grade guideline

Confidence in the RfD:

Study: Medium Data Base: High RfD: Medium

The critical study appears to be of fair quality and is therefore given a medium rating. Confidence in the data base is high and therefore the RfD is given medium confidence rating.

Documentation of RfD and Review:

Registration Files

Agency RfD Review:

First Review: 9/02/86
Second Review:
Verification Date: 9/02/86

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