4-29-86 CASWELL FILE

REFERENCE DOSES (RFDs) FOR ORAL EXPOSURE

Chemical: Fonofos (Dyfonate)

CAS #: 944-22-9
Caswell #: 454B

Carcinogenicity: Oncogenic potential undetermined.

Systemic Toxicity: See below.

Preparation Date: 4/29/86

Endpoint	Experimental Doses	UF	MF	RfD
Woodard Research Corp. 1969	0.2 mg/kg/day NOEL	100	-	0.002 mg/kg/day
2-Year Dog Feeding Study	1.5 mg/kg/day LEL			
moderate RBC ChE inhibition, increase in liver weight, microscopic changes in liver and small intestine, tremors, lacrimation, and salivation				

Endpoint and Experimental Doses:

Woodard Research Corp.
2-Year Dog Feeding Study
January 9, 1969

Groups of purebred beagle dogs, 4 males and 4 females per group, were fed 0, 0.2, 1.5, and 12 mg/kg/day fonofos (dyfonate) in diets for 2 years. The following effects were observed at 1.5 mg/kg/day: moderate inhibition of blood cholinesterase, an increase in liver weight, and tremors. At 12 mg/kg, there were an increase in liver weight, and tissue reactions (microscopically) in the small intestine and liver. No compound related effects were observed at 0.2 mg/kg/day.

Uncertainty Factors (UFs):

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

Modifying Factors (MFs):

An additional MF of 10 was not considered necessary even though the data base is not complete, since the data at hand allows the conclusion that the additional or repeat studies are not likely to provide a substantially more sensitive toxicological endpoint.

Additional Comments:

The 2-year rat feeding study was not used to derive the RfD because of the equivocal ChE depression observed. The cholinergic and systemic effects observed in the dog, the NOEL in this species, and the appropriate UF provided overall a better basis, and a more conservative level for an RfD.

Data Considered for Establishing the RfD

1) 2-Year Feeding - Dog (NOEL = 0.2 mg/kg; LEL = 1.5 mg/kg, increase liver weight, tremors, lacrimation, salivation and ChE inhibiton; minimum)

2) 2-Year Feeding/Oncogenic - Rat (ChE NOEL = 0.5 mg/kg; ChE LEL = 1.58 mg/kg, plasma and RBC ChE inhibition, Brain ChE inhibition at 0.5 mg/kg/day (LEL); supplementary)

3) 3-Generation Reproduction - Rat (Fetotoxic NOEL > 1.58 mg/kg (HDT); minimum)

4) Teratology - Mice (Fetotoxic NOEL = 2 mg/kg; Fetotoxic LEL = 6 mg/kg, sternebrae malalignment and slight dilation of 4th cerebral ventricules, minimum)

Data Gap(s)

1) 2-Year Feeding/Oncogenic Rat Study
2) Rat Teratology Study
3) Rabbit Teratology Study

Other Data Considered

Confidence in the RfD:

Study: Medium Data Base: Low RfD: Medium

The critical study appears to be of fair quality and is given a medium confidence rating. Since the data base for chronic toxicity is complete, the RfD is given a medium confidence rating.

Documentation of RfD and Review:

Registration Standard, August 1983
Registration Files

Agency RfD Review:

First Review: 6/24/86
Second Review:
Verification Date: 6/24/86

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