2/3/87

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REFERENCE DOSES (RFDs) FOR ORAL EXPOSURE

Chemical: Curacron/Profenofos

CAS #: 41198-08-7
Caswell #: 266AA

Carcinogenicity: No evidence of oncogenicity in two adequate animal (mouse and rat) studies.

Systemic Toxicity: See below.

Preparation Date: 2/19/87

Endpoint	Experimental Doses	UF	MF	RfD
Ciba-Geigy Limited (1981)	0.2 ppm (0.005 mg/kg/day) RBC and Plasma NOEL	100	—	0.00005 mg/kg/day
6-Month Dog Feeding Study	2.0 ppm (0.05 mg/kg/day) RBC and Plasma LEL			
plasma and RBC cholinesterase inhibition				

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

Endpoint and Experimental Doses:

6-Month Toxicity Study with Dogs
Ciba-Geigy Limited
Study No. 790804

Groups of 7 male and 7 female beagle dogs were fed dosage levels of 0, 0.2, 2, 100, or 500 ppm daily for 182 days (26 weeks). One animal per sex per and dose group was maintained on laboratory chow only for a 1-month posttreatment recovery period. The only significant adverse effect produced by curacron in male and female dogs during the 6-month study was inhibition of plasma and RBC cholinesterase activity at 2, 100 and 500 pmm doses. Brain activity was determined at 26 weeks of test on 6 male and 6 female dogs; one each from each dose level. Males - the only brain ChE inhibition was 5% at the 2.0 ppm dose level; Females - 8% brain ChE inhibition at the 0.2 ppm dose level, 10%, 11% and 5% brain ChE inhibition at the 2, 100 and 500 ppm dose levels respectively.

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Uncertainty Factors (UFs):

An uncertainty factor of 10 was used to account for the cholinesterase inhibition extrapolation from animal to man and an additional UF of 10 to account for brain cholinesterase inhibition ~~at the lowest dose tested.~~ for the fact that the determination of at the treatment levels was unreliable and a NOEL for this endpoint could not be ~~deduced~~ reduced

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Modifying Factors (MFs):

None

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Additional Comments:

Data Considered for Establishing the RfD

1) 6-Month Feeding - Dog Plasma NOEL = 0.2 ppm (0.005 mg/kg/day); LEL = 2 ppm (0.05 mg/kg/day); RBC NOEL (M) = 0.2 ppm, RBC LEL = 2.0 ppm; RBC NOEL (F) = 2.0 ppm; LEL = 100 ppm (2.5 mg/kg/day); Core grade minimum

2) 2-Year Feeding/Oncogenic - Rat ChE NOEL = 0.3 ppm (0.015 mg/kg/day), ChE LEL = 10 ppm (0.5 mg/kg/day); Systemic NOEL > 100 ppm (5 mg/kg/day)(HDT); Core grade minimum

3) 3-Generation Reproduction - Rat ChE NOEL = 1.0 ppm (0.05 mg/kg/day), ChE LEL = 20 ppm (1 mg/kg/day)(decreased RBC ChE in M and F; decreased plasma ChE in F); Reproduction NOEL $\geq$ 20 ppm (HDT); IBT valid, Core grade minimum

4) Teratology - Rat Maternal NOEL = 90 mg/kg, Maternal LEL = 120 mg/kg (HDT; weight loss and mortality); Fetotoxic NEOL > 120 mg/kg; Teratogenic NOEL > 120 mg/kg (HDT); Core grade guideline

5) Teratology - Rat Teratogenic NOEL > 60 mg/kg (HDT); Maternal NOEL = 30 mg/kg, Maternal LEL = 60 mg/kg (decreased food consumption); Fetotoxic NOEL > 60 mg/kg/day (HDT); Core grade guideline

6) Teratology - Rabbit Maternal NOEL = 30 mg/kg, Maternal LEL = 60 mg/kg (decreased body weight); Teratogenic and Developmental NOEL > 175 mg/kg (HDT); Core grade minimum

Data Gap(s)

None

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Other Data Considered

1) 2-Year Feeding/Oncogenic - Mice ChE NOEL = 1.0 ppm (0.15 mg/kg/day), ChE LEL = 30 ppm (4.5 mg/kg/day)(> 20% RBC and plasma inhibition); Systemic and Oncogenic NOEL > 100 ppm (15 mg/kg/day)(HDT); Core grade minimum

2) 90-Day Feeding - Rat ChE LEL $\leq$ 3 ppm (0.15 mg/kg/day)(lowest level fed; depressed ChE activity); Core grade minimum

3) 90-Day Feeding - Dog Systemic NOEL > 200 ppm (5 mg/kg/day); ChE LEL < 2 ppm (0.05 mg/kg/day)(RBC ChE inhibition); IBT valid)

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Confidence in the RfD:

Study: Medium Data Base: High RfD: High

The critical study is of good quality and is given a medium confidence rating. Additional studies are supportive and of good quality, therefore the RfD is given a high confidence rating.

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Documentation of RfD and Review:

Registration Files

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Agency RfD Review:

First Review:
Second Review:
Verification Date:

U.S. EPA Contact:

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