US EPA ARCHIVE DOCUMENT
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

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Experimental Doses</th>
<th>UF</th>
<th>MF</th>
<th>RfD</th>
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</thead>
<tbody>
<tr>
<td>Ciba-Geigy Limited (1981)</td>
<td>0.2 ppm (0.005 mg/kg/day)</td>
<td>100</td>
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<td>0.00005 mg/kg/day</td>
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<td>RBC and Plasma NOEL</td>
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<tr>
<td>6-Month Dog Feeding Study</td>
<td>2.0 ppm (0.05 mg/kg/day)</td>
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<td>RBC and Plasma LEL</td>
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<td>plasma and RBC cholinesterase inhibition</td>
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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 ppm doses. Brain activity was determined at 26 weeks of test on 5 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.
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. A NOEL for this endpoint could not be established.

Modifying Factors (MFs):

None

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 ≥ 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 NOEL > 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
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 < 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

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.

Documentation of RfD and Review:

Registration Files

Agency RfD Review:  U.S. EPA Contact:
First Review:  Primary: George Ghali FTS 557-7490
Second Review:  Secondary: Reto Engler FTS 557-7491
Verification Date: