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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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MEMORANDUM

TO: Marilyn Mautz (16)
Registration Division (TS-767)

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

THRU: Orville E. Paynter, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: Review of Acute Toxicology Studies for Curacron
Acc. No. 247933 CASWELL#266AA

Registrant: Ciba-Geigy Corporation
Agricultural Division
P.O. Box 11422
Greensboro, North Carolina 27409

Recommendation:

It is recommended that the submitted studies be classified as follows:

1. Acute Dermal
Core Guidelines.
Dermal LD_{50} are 146.8, 143.39, 97.54 and 15.92 mg/kg for intact males and females and abraded males and females, respectively.
Toxicity Category I, Danger

2. Acute Inhalation
Core Guidelines. LC_{50} is 3.36 mg/L. Toxicity Category III, Caution.

3. Eye Irritation
Minimal, reversible irritation, no corneal opacity.
Toxicity Category III, Caution.

4. Skin Irritation
Core Guidelines. Slight irritation. Toxicity Category IV

It is also noted that the proposed label, with revisions based on these studies, is acceptable as submitted.

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Review of Data:

1. Acute Dermal Toxicity. Rabbits. Conducted at Stillmeadow, Inc., Houston, Texas, Project No. 2460-81; April 2, 1982 and submitted by Ciba-Geigy.

Five male and 5 female New Zealand white rabbits were dermally treated with technical Curacron. Test Material was applied to the clipped trunks of animals with intact skin or with skin abraded. The following dosages were used for intact or abraded skin:

Dose (mg/kg)	Number Tested	
	Males	Females
Intact		
88.8	-	5
133	5	5
163	5	-
200	5	5
Abraded		
72.6	5	-
88.8	5	-
109	5	5
133	5	5
163	-	5
200	5	5
500	5	5
2000	5	5

The trunk of each animal was wrapped with polyethylene film after treatment. After 24 hours, test material and wrappings were removed and observations were recorded at 0.5, 3, 6 hours and daily for 14 days after treatment. A gross necropsy was conducted on each animal after 14 days.

Results:

The dermal LD_{50}s are as follows: Male (Intact) 146.8 mg/kg, Male (Abraded) 97.54 mg/kg, Female (Intact) 143.39 mg/kg and Female (Abraded) 159.2 mg/kg. Clinical observations of toxicity included ataxia, tremors, constricted pupils, diarrhea, lacrimation, decreased activity, salivation, ptosis, small feces and lack of urination or defecation. Gross necropsy observations of toxicity included pronounced serosal blood vessels on the stomach and small

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intestine and discoloration of contents, empty or distended gastrointestinal tract, discoloration of the lungs, liquid in phenral cavity, cysts on the kidney and signs of diarrhea, lacrimation or salivation.

Very slight erythema and edema was observed in all groups of animals with intact skin. Groups with abraded skin had erythema and edema ranging from very slight to well defined erythema and slight edema.

Core Classification: Core Guidelines.

Dermal LD_{50} are 146.8 and 143.39 mg/kg intact males and females, respectively, and 97.54 and 159.2 mg/kg, abraded males and females, respectively. Toxicity Category I, Danger.

2. Acute Inhalation Study, Rats. Conducted at Toxigenics, Inc., Decatur, Illinois, Study No. 420-0921, June 29, 1982 and submitted by Ciba-Geigy.

Four 4-hour exposures to technical Curacron were conducted in a 500 liter stainless steel and glass inhalation chamber. Each exposure utilized 5 male and 5 female Charles River adult rats. Time weighted average actual concentrations were 2.23, 2.77, 4.57 and 6.30 mg/L. The average mass median diameter of the aerosol was 2.04 micrometers. Observations of animals were recorded at least every 30 minutes during exposure and twice daily during the 14 day post exposure observation period. After 14 days, all animals were sacrificed by CO_2 asphyxiation and subjected to a gross necropsy conducted under the supervision of a pathologist.

Results:

The LC_{50} was calculated to be 3.36 mg/liter. Clinical observations of toxicity included damp fur, irregular breathing, poor coat quality, crusty muzzle, stained fur, alopecia, salivation, lacrimation, gasping andd tremors. Gross necropsy findings of toxicity included granular discoloration of the lungs and stomach.

Core Classification: Core Guidelines.

The LC_{50} was calculated to be 3.36 mg/liter (Tox. Cat. III).

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3. Eye Irritation, Rabbits. Conducted at Stillmeadow, Inc., Houston, Texas, Project No. 2461-81, January 20, 1982 and submitted by Ciba-Geigy Corporation.

One tenth of an ml of technical Curacron was placed into the conjunctival sac of 9 albino rabbits. The treated eye of 3 of the rabbits were washed 30 seconds after treatment. The treated eyes were examined after 1, 24, 48 and 72 hours and at 4 and 7 days after treatment. Corneas were examined with fluorescein sodium one hour after treatment and for each remaining intervals until staining of the cornea was absent.

Results:

Corneal opacity was not observed in any animal. Minimal redness, chemosis and/or discharge were observed; however, all signs of toxicity were absent by day 7.

Core Classification: Core Guidelines.

Minimal irritation, reversible within 7 days, corneal opacity not induced. Toxicity Category III.

4. Skin Irritation, Rabbits. Conducted at Stillmeadow, Inc., Houston, Texas, Project No. 2462-81, January 29, 1982 and submitted by Ciba-Geigy.

Six New Zealand white rabbits were dermally exposed to technical Curacron. The trunks of animals were shaved and the stratum cornea was abraded. One half ml of test material was applied to each animal on 4 test sites (two intact and two abraded) and covered with a surgical gauze pad and a polyethylene film. Twenty-four hours after treatment, patches and test material were removed. Initially and after 72 hours, animals were observed for edema, erythema and other signs of irritation.

Results:

Two animals died within 24 hours, two more animals died prior to 48 hours. After 24 hours, edema and erythema were either absent or very slight. The mean irritation score after 24 hours indicated "slightly irritating" for both intact and abraded skin.

Core Classification: Core Guidelines.

Slight irritation, Toxicity Category IV.

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5. Skin Sensitization, Guinea Pigs. Conducted at Stillmeadow, Inc., Houston, Texas, Project No. 2463-81, March 3, 1982 and submitted by Ciba-Geigy.

Ten male adult short-tailed albino guinea pigs were treated interdermally with a 0.01% solution of technical Curacron in 0.9% saline on day 0, 2, 5, 7, 9, 12, 14, 16, 19, 21 and 35. Compound application was made on adjacent skin test sites. Ten addition animals were similarly treated with 0.50% of 2,4-dinitrochlorobenzene in 0.9% saline. Observations were made after 24 and 48 hours for each test site.

Results:

Sensitizing reactions were produced by both test material and positive control. Significantly increased skin irritation was found both in the positive control ($p < .01$) and test groups ($p < .05$) upon comparison of the degree of irritation of the initial and final applications.

Core Classification: Core-Minimum.

Curacron technical appears to be a potential sensitizing agent.

Gary J. Burin LDC 10/19/82
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Hazard Evaluation Division (TS-769)

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