UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE 6-26-80

SUBJECT: EPA File No. 10182-EI 10182-EO, Teratology Studies with Brodifacoum and Resubmission of Pesticide Applications for Registration.

FROM: John Doherty 6/18/80
Toxicology Branch/HED (TS-769)

TOX Chem. #114AAA

TO: Dan Peacock, PM Team #16
Registration Division (TS-767)

Conclusion:

1. Toxicology Branch has no further objections to the registration of these products for formulating use only.

2. The two teratology studies submitted, meet current EPA requirements. No teratogenic effects were noted at doses up to 20 mg/kg in the rat and 5 mg/kg in the rabbit.

3. These tests emphasize the extreme toxicity of brodifacoum.

Action Requested:

The registrant is seeking to register the following two products:

1. EPA File No. 10182-EO Brodifacoum Technical

Active Ingredient (Brodifacoum)	90%
Inert	10%
	100%

2. EPA File No. 10182-EI Brodifacoum Concentrate

Active Ingredient (Brodifacoum)	0.25%
Inert	99.75%
	100.00%

The package sent to Toxicology Branch contains:

a) The proposed labels,
b) Teratology studies with rats and rabbits.

(These studies are in EPA Acc. No. 242118 and 242119).

Review of Studies Submitted

1. Brodifacoum: Teratology Study in the Rat.

Central Toxicology Laboratory, ICI Ltd., Issued January 22, 1980; Report No. CTL/P/437.

Four groups of Wistar-derived female rats, 30 per group, mated with males of the same strain, and then grouped and dosed with 0,0.001, 0.01, or 0.02 mg/kg brodifacoum in 10% v/v aqueous ethanol. Dosing was orally on days 6-15 inclusive of pregnancy. A preliminary screening test determined the doses to be used.

Results:

A. Maternal effects - There were no deaths, uteri of three females in the high dose group had blood. Weight gain was not adversely effected. 25 controls, 26 low dose, 27 mid dose, and 24 high dose dams became pregnant, and produced litters. The test chemical did not affect the various parameters of the litters produced.

B. Pup data - Foetal weight and litter weight were not affected. No differences were noted in soft tissue examinations. Some differences were noted in skeletal examination but these indicated a slightly better degree of ossification in development.

Conclusion:

This study is Core Minimum. No positive control was included. The raw data are not included and data are in summary tables only.

2. Brodifacoum: Teratogenicity Study in the Rabbit.

Central Toxicology Laboratory, ICI Ltd., Issued January 30, 1980; Report No. CTL/P/459.

Five groups of 15 female Dutch rabbits were mated with proven bucks. Following mating, a dose of chorionic gonadotropin was administered to promote ovulation. Brodifacoum was disolved in a solution of 5% v/v aqueous ethanol and three groups were treated with .001, .002, and .005 mg/kg at the rate of 2 ml/kg. Two control groups were run, 0.5% ethanol and 0.5% tween 80. No positive control group was included. Dosing was on days 6-18 inclusive of the gestation period. The dams were sacrificed on day 29.

Results:

A. *Effects on dams - 10 of 15 high dose group rabbits died of internal hemorrhage that was related to the test chemical. Deaths in the low and mid dose groups were not stated as being related to the test chemical.*

8 ethanol controls, 10 low dose, 11 mid dose, 3 high dose, and 11 tween 80 control females had pregnancies that went to term. Other than deaths at the high dose, the test chemical did not appear to adversely affect the females with respect to production of litters.

B. *Litter data - No adverse effects on external development, soft tissue development, or skeletal development were reported.*

Conclusion:

This study is Core Minimum. No positive control was included. The data are presented in summary tables only. No raw or individual animal data as presented.

OPP:HED:TOX: J.DOHERTY:sb 6/13/80 X73710 TS-769 Rm. 814 CM 2 #8

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