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SUBJECT EPA Reg. No. 432-487; Technical Resmethrin (SBP-1382); Review of Rabbit Teratology Study

TOX. Chem. No. 83E

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TO F. D. R. Gee, PM #17
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Action Requested:

Review rabbit teratology study to support registrations/tolerances with resmethrin.

Conclusion:

This study has been classified as Core Minimum and demonstrates that resmethrin does not induce teratogenic effects in rabbits at dose levels up to and including 100 mg/kg.

Remarks:

Resmethrin treated dams at all doses are reported as having pups with "dark livers". The testing laboratory describes this as a possible fetotoxic effect-despite the fact that there was no dose dependence relationship observed. Toxicology Branch accepts this interpretation of a possible fetotoxic effect at the lowest dose tested (10 mg/kg). It is apparently a species related effect because a teratology study in rats with the same test material did not demonstrate a similar lesion (see review by John Doherty, EPA Reg. No. 432-487, dated 6/26/80).

Detailed Review of Study

Identification of Study:

"Teratologic Evaluation of SBP-1382 Technical in Albino Rabbits"

Food and Drug Research Laboratories, Inc.; Report No. 6288; October 31, 1979; EPA Accession No. 241800.

Protocol:

5 groups of 20 pregnant female New Zealand White Minnikin rabbits (a hybrid strain resulting from the cross of New Zealand White and Dutch-Belted rabbits) were dosed orally with either 0, 10, 30, or 100 mg/kg of technical resmethrin [(5-Benzyl-3-furyl) methyl 2,2-dimethyl-3-(2-methylpropenyl)cyclopropanecarboxylate, 90%], or 2.5 mg/kg of 6-aminonicotinamide (6-AN) in corn oil. Resmethrin was administered on days 6 through 18 of gestation. The positive control (6-AN) was administered only on day 9 of gestation. On day 29 of gestation, all females were sacrificed and their fetuses subjected to examination.

Results:

A. Maternal and Reproductive Effects.

1. The lowest % pregnancy was in the control group (70%). The % pregnancy in the test group dams was 75-90%.

2. There was no apparent effect of resmethrin on body weights of the test dams.

3. No overt toxic effects (general appearance or behavior) were noted.

4. At all doses of resmethrin treated dams, there was a decreased percentage of implants resulting in live fetuses and an increased percentage of resorption sites. Although these parameters were different from the control, they did not show a change with increasing dose.

5. The average number of live fetuses per test dam was comparable to controls. Neonatal survival was not adversely affected.

There is apparently a discrepancy between the summary table and the discussion related to dam reproduction data. The summary table states that 15 of 18 positive control dams and 16 of 16 high dose group dams had pregnancies that went to term. However, the same table states that 9 of 18 positive control and 3 of 16 high dose group dams had litters completely resorbed. This discrepancy should be clarified.

B. Effects on the Fetuses.

1. Soft tissues - The only remarkable finding was an increase in "dark livers" for all doses of rabbits treated with resmethrin. This anomaly did not demonstrate a dose dependent effect. It is considered, however, to be a possible fetotoxic effect.

	% of Fetuses with "Dark Liver"	Incidences/Litters Effected
Negative Control	0%	0/0
10 mg/kg	23%	13/4
30 mg/kg	17%	14/4
100 mg/kg	14%	8/3

2. Skeletal findings - The high dose group exhibited an increase in fused and extra sternebrae that was statistically significant. This finding is a frequent observation in teratology studies and is considered to be an effect due to stress rather than a teratogenic effect.

C. The Positive Control.

1. 6-amimonicotinamide induced a variety of expected abnormalities in the fetuses.

Discussion:

This study is Core Minimum.

This study could be upgraded if an explanation for the discrepancy in dam reproduction data (described above) is provided by the registrant or testing laboratory.

OPP:HED:TOX: J.DOHERTY:sb 5/14/80 X73710 TS-769 Rm. 814 CM 2 #8