

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: November 28, 1979

001908

SUBJECT: EPA Reg. No. 432-487, Three-Generation Reproduction Study (Rats) with Resmethrin (SBP-1382 Technical). Caswell #83E

FROM: John Doherty *John Doherty 11/21/79*
Toxicology Branch/HED (TS-769) *B. Ad 11/29/79*

TO: F. D. R. Gee, Product Manager #17
Registration Division (TS-767)

Action Requested:

Review three-generation reproduction study with resmethrin (technical) and determine if study meets EPA standards to support the safety of resmethrin. This study is in EPA accession #240984.

Conclusion:

1. The study has been reviewed and classified as CORE GUIDELINES.
2. The data in the study do not support a NOEL of 500 ppm (the lowest dose level tested). Statistically significant increases in percent of F3B pups cast dead and decreases in the mean body weights of the pups at weaning were observed at the 500 ppm dose level.
3. EPA regulations require that a NOEL be established for a reproduction study. Therefore, a second study will have to be submitted in order to establish a NOEL.

Detailed Review of Study:

The Evaluation of the Effects of SBP-1382 Following Dietary Administration Through Three-Generations in Sprague-Dawley Rats.

Food and Drug Research Laboratories; July 13, 1979. (Laboratory No. 5739).

Protocol:

Four groups of 20 male and 20 female rats each were given diets containing 0, 500, 800 or 1250 ppm of resmethrin (technical contained 90% active ingredient). These groups were labelled the F0 generation and were mated to produce first an F1A generation and were subsequently remated to produce a F1B generation. Twenty rats per sex were selected from the F1A group to be mated to produce F2A and F2B generations. Twenty rats per sex from the F2A generation were mated to produce F3A and F3B generations.

Results:

1. Fertility indexes and gestation indexes did not show compound related effects at any dose.
2. Viability indexes (pups that survived to 4 days) were adversely affected at 800 ppm and 1250 ppm - being more serious at 1250 ppm.
3. Lactation indexes, as indicated by both pup survival to 21 days and by dam efficiency, were not affected at any test dose.
4. Mean litter size at birth (number of pups per litter) was not affected at 500 ppm. At 800 ppm, the F1B litter was depressed. At 1250 ppm, F1B, F2A and F3A litters were depressed.
5. Pups cast dead. The 500 ppm group had a single incidence of a statistically significant increased parameter for the F3B generation. This was in a progression of 1.2% (3/244 for 0 ppm), 4.3% (12/282 for 500 ppm), 4.5% (11/246 for 800 ppm) and 7.7% (19/246 for 1250 ppm). At 800 and 1250 ppm all generations except F3A for 800 ppm were statistically increased over the controls. This significant difference and obvious trend does not support a NOEL of 500 ppm. See attached table.
6. Mean litter weights at birth and at 4 days were adversely (lower weights) affected at 1250 ppm and possibly lower ~~in weight~~ at 800 ppm.
7. Mean pup weights at weaning. All litters of the 500 ppm group had lower mean pup weights at weaning than the controls (except F3B). F1A, F1B and F3A litters were statistically significantly lower. All generations in the 800 and 1250 ppm groups were also statistically significantly lower in weight. A progressive dose response decrease is supported. See attached table.
8. Mean weekly body weights and food consumption were tabulated for F0, F1A and F2A adult groups. Adverse effects (depression) were noted at 800 and 1250 ppm.
9. Mean dam body weight during lactation. Highest dose level dams only were adversely affected.
10. General observations. None are reported that do not also appear in the controls.
11. Gross pathology (on 80 males and 80 females of the F2A generation as adults). Did not reveal tumors or other gross morphologic evidence that was considered by the pathologist (George E. Cox) to be compound related.

Conclusions:

A CORE GUIDELINES study. The occurrence of statistically significant deviations related to an increase in pups cast dead and lower mean pup weights at weaning in the 500 ppm group prevent Toxicology Branch concurrence with the laboratory's assertion that the NOEL is 500 ppm. The NOEL is < 500 ppm.

Attachment:

EPA:OPP:HED:TOX:RD BUDD:sb 11/26/79 X77395

*see the
unsubstituted*