



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

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OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCESMEMORANDUM

DATE: October 21, 1982

TO: Edwin R. Budd and John Doherty  
Toxicology Branch  
Hazard Evaluation Division (TS-769)

SUBJECT: FAP 9H5210 and EPA Reg. No. 432-487  
Statistical Review of Thomas E. Norwood Re-analysis  
3-Generation Rat Reproduction Study with Resmethrin

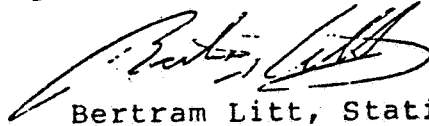
The techniques currently used to analyze multigeneration reproductive studies are inadequate in that they fail to consider the study as a unified entity that is to say that the design of the study is not used as the basis for statistical analysis. For each measure of success, say mortality by the end of day 4, the statistic used should include results from each generation. This review is not the place to make new policy, and therefore Dr. Norwood's use of mathematical extrapolation of study data to zero-response levels is not admissible. Even if the policy were acceptable, no evidence is furnished to establish that the log-probit is an appropriate model for any of the study responses.

The technique used by Dr. Norwood to estimate standard errors is reasonable, at least for proportion of pups cast dead or dead by end of day 4 and here we agree that the suggested method seems appropriate. It is less clear that this applies equally well to continuous data. The use of 'T tests' in this sort of experiment is less than optimal. TOX Branch accepts the use here as prevailing state-of-the-art. On that basis any single  $p = .05$  might be a chance occurrence as we expect approximately 5 false positives out of 100 independent tests. But 2 tests on the same parameter would be  $.05 \times .05 = .0025$  or a very rare event indeed. In this experiment Dr. Norwood shows in Table V that the mean body weight for pups at weaning, or 21 days, was statistically significantly lower in the 500 ppm Resmethrin fed animals in the F<sub>1</sub>B ( $52.9 \pm 1.3$ ) and the F<sub>3</sub>A ( $49.3 \pm 1.3$ ) generations compared to the control animals ( $56.5 \pm 1.2$  and  $53.9 \pm 0.8$  respectively).

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No other findings at the 500 ppm dose level are reported to be statistically significant. In so far as it is possible to verify what was done I concur with the results of Dr. Norwood's individual statistical tests for the data from this Resmethrin 3-generation study in rats.



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