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SUBJECT: Validation Review of IBT Study No. J-238 Teratogenic Study with Bladex in Albino Rabbits

FROM: Larry Anderson
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James [unclear]

William S. Butler for M. Adrian Gross

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Discussion

It is concluded that this study should be considered an invalid estimate of the fetotoxic/teratogenic potential of Bladex in rabbits. Reasons for this conclusion include the following:

1. In the initial test the rate of conception following artificial insemination of does was poor in all dosage groups (vehicle control, positive control, test groups given 0.32, 1.0, or 3.2 mg/kg/day Bladex). Because of insufficient numbers of pregnant animals, the test was repeated. In this second test there was a problem with animals dying presumably from pneumonia. Therefore, a third study was used to evaluate the mid dose test group. Vehicle and positive control data were ultimately obtained from other studies. Basically, intra- and inter-group data were not derived from animals concurrently on study. To this reviewer, this practice is not acceptable in a teratology study.
2. Twenty seven does died with a rather even distribution among the 5 dosage groups. Observations on these animals reflect a predominance of respiratory problems, e.g., "lungs filled with pus". These findings could be indicative of inadequate animal husbandry or improper dosing technique by gavage. These deaths were not identified in the final report.
3. According to raw data, 3 abortions were found in each of the vehicle control, low dose, and mid dose groups. However, only 2 and 1 abortions in the low and mid dose groups, respectively, were reported.