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

MAY 28 1982

003001

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: William Miller (16)
Registration Division (TS-767)

SUBJECT: Addendum to Validation and Review of Additional
Histopathology Data for IBT Three Generation
Reproduction Study of Curacron-in-Albino Rats;
IBT No. 623-079244 *BS* CASWELL#266AA
Accession No. 247456

Registrant: Ciba-Geigy Corporation
Agricultural Division
P.O. Box 11422
Greensboro, North Carolina 27049

Background Information:

The validation of this study performed on March 22, 1982 by this reviewer noted, as the #1 deficiency, that the number of tissues examined microscopically could not be verified by the raw data. It also noted that "... if a tissue inventory indicates that all required tissues are present and histopathology observations can be confirmed through reexamination of tissue... an upgrading of this study to valid may be possible." The registrant has recently submitted a report containing the findings of microscopic examination of all available slides for this study. The report consists of the findings reported by Experimental Pathology Laboratories on January 12, 1981 (examination of lung, trachea, testes, epididymides, ovaries, and uterus) and the recent findings resulting from examination of all other available slides.

Recommendation:

As a result of the recent submission, it is recommended that the classification of this study be upgraded to Valid, Core-Minimum. Compound related histological effects were not observed at any dose level and the NOEL levels remain at 1.0 ppm for cholinesterase depression and > 20 ppm for reproductive and systemic effects.

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Discussion:

A review of the histopathological evaluation, performed by Experimental Pathology Laboratories and submitted to Ciba-Geigy on April 29, 1982, indicates that protocol required tissues were generally present for scheduled sacrifice animals of the control and T-III dose levels of the F₀, F₁, F₂ and F_{3b} generations. Missing tissues for those animals were generally limited to pituitary gland, peripheral nerve, and other tissues which are easily lost (with the exception of animal no. 79 of the F₀, T-III group, a scheduled sacrifice animal for which many tissues were inexplicably autolyzed). Of the animals dying on test, many of the required tissues were too badly autolyzed to permit diagnosis. However, a sufficient number of tissues and animals were examined to satisfy study requirements.

No compound related histological alterations were observed in the reexamination of all available slides.

Gary J. Burin

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