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

MEMORANDUM

10/21/82

002236

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: Marilyn Mautz (16)
Registration Division (TS-767)

THRU: Orville E. Paynter, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: Comments on Curacron Neurotoxicity Including the Evaluation of a Validated Acute Neurotoxicity Study in Chickens, IBT#8580-111870 CASWELL#266AA

Registrant: Ciba-Geigy Corp.
Agricultural Division
P.O. Box 11422
Greensboro, North Carolina 27409

Action Requested:

Evaluation of validated IBT Study No. 8580-111870 and reconsideration of the need for additional neurotoxicity testing. The study has been validated by HPB Canada and classified as Supplementary Data.

Recommendation/Discussion:

It is recommended that this study be reclassified as Core Supplementary Data. As per the review of this study on July 16, 1980 from W. Woodrow, no delayed neurotoxicity was noted in birds treated with this chemical. However, the requirement noted in the letter of May 13, 1982 from L. Chitlik that Ciba-Geigy "provide an acceptable (neurotoxicity) study by 6/1/83" has not yet been satisfied. Although 3 acute delayed neurotoxicity studies have been submitted by the registrants, no individual study has attained Core-Minimum status.

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Review of Data:

Acute Delayed Neurotoxicity, Chickens. IBT No. 8580-11187, July 25, 1978. Submitted by Ciba-Geigy.

(This study was validated by Dr. Davies of HPB Canada in November, 1980 and classified as Supplementary Data on the basis of the following:

1. Lack of an adequate challenge dose.

2. Lack of atropine pretreatment.

3. Lack of confirmation of animal age.

4. Lack of confirmation of mortality data for the LD_{50} stage.)

See review of July 16, 1980 from Woodrow for a discussion of study protocol.

Results:

Clinical observations or microscopic findings of acute delayed neurotoxicity were not observed in animals receiving Curacron or corn oil. All positive control birds delayed clinical symptoms and showed microscopic findings of acute delayed neurotoxicity.

Discussion:

Lack of atropine pretreatment contributed to a high mortality rate observed after initial dosing (at 30 mg/kg and 45.7 mg/kg). The second dosing was conducted at 17.1 mg/kg, a level less than the LD_{50}. Thus both exhibited dosings may not have been conducted at appropriate dose levels.

In addition, test animal age could not be verified, as noted in the validation. Although the registrant states that the deficiencies noted in validation are evaluative, the issue becomes moot during this review as the issues of lack of adequate dosing or use of animals of maximum sensitivity are clearly ones that must be resolved before a study attains a Core-Minimum classification.

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Core Classification:

Supplementary Data due to deficiencies in dosing and animal sensitivity per the Canadian validation of June 4, 1982. Per the review of July 16, 1980 from W. Woodrow, no delayed neurotoxicity was observed in animals administered Curacron.

Gary J Burin 10/21/82

Gary J. Burin, Toxicologist
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