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

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: W. Miller, PM#16
Registration Division (TS-767)

FROM: Amal Mahfouz, Ph.D.
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Amal Mahfouz 1/24/84

THRU: Laurence D. Chitlik, DABT
Section Head, Section V
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1/25/84

William L. Burnam, Chief
Toxicology Branch
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1/30/84

SUBJECT: Oftanol (Isofenphos). An Interim Report Concerning Isofenphos, Antidotes and Delayed Neurotoxicity, by Barry W. Wilson.

We are forwarding to you the following items which we have just received from Dr. Barry Wilson of the University of California in response to our previous inquiries relative to his findings on Oftanol delayed neurotoxicity:

1. A letter dated January 18, 1984 from B. Wilson to L. Chitlik (TOX Branch).

2. A letter dated January 18, 1984 from B. Wilson to D.J. Clegg, (Bureau of Chemical Safety in Canada).

3. A letter dated December 28, 1983 from B. Wilson to Rex Magee of the California Department of Food and Agriculture.

4. An Interim Report dated December 1983; Title: Antidotes and Isofenphos, by B.W. Wilson.

We note that the findings reported in Dr. Wilson's Interim Report (#4 above) concerning Oftanol delayed neurotoxicity and antidotal effects were previously summarized in his memo to Rex Magee on November 21, 1983. Our memos of 12/7/83 and 12/28/83 elaborately addressed these findings.

We also note that Dr. Wilson's studies were primarily geared to investigate the antidotal effect in Oftanol exposed hens and rats; his findings concerning the protective effects of the antidotes in both species were similar to the previously submitted registrant's data.

However, the main usefulness of Dr. Wilson's data is his delayed neurotoxicity findings in protected hens treated with Oftanol. His data were positive at an oral dosage level of 75 mg/kg while the registrant's data were negative at this level. Also Wilson's data reflected a much lower value for the oral LD50 in unprotected hens (5 mg/kg) than the registrant's LD50 (21 mg/kg). These facts justifed our reassessment of the delayed neurotoxicity data for Oftanol which were previously submitted by the registrant, see our memos of 12/7/83 and 12/28/83.

In conclusion, Dr. wilson's data did not provide enough information in order to adequately evaluate the Oftanol delayed neuropathy; and to attain this goal, the following data should be submitted by the registrant within a reasonable time:

- An acute delayed neurotoxicity study in hens (with a repeated dosage of Isofenphos for any 21-day survivors of an initial appropriate dosage of Oftanol).
- A Subchronic 90-Day Neurotoxicity Study in Hens.
- All individual bird data for the submitted NTE activity study (Mobay's Report #80678, 4/19/83, Study #3007376)
- Any additional information available to, or in possession of the registrant relative to Oftanol neurotoxicity.

The above requested 2 new studies (acute and subchronic) should be performed in the most sensitive strain of chicken, and should include NTE determinations using an appropriate method. We anticipate that the histopathological investigation on the target nerve tissues will be adequately conducted.

Attachment (4)