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TR-4302

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

004302

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: EPA Reg. No. 476-2134. Dyfonate (Fonofos).
Registrant's Response to Registration Standard.

Tox Chem. No. 454B

FROM: Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769) Budd 2/19/85

TO: W. H. Miller, Product Manager #16
Registration Division (TS-767)

Action Requested:

The registrant, Stauffer Chemical Company, in a letter dated September 17, 1984, has submitted a response to the Dyfonate Registration Standard. With regard to issues involving the review of toxicology studies, Stauffer submitted the following for consideration by EPA.

1. Additional information and comments on the mouse teratology study (T-10192), including a copy of a letter from William J. Scott, Jr., D.V.M., Ph.D. (Professor of Research Pediatrics, Children's Hospital Medical Center) to J. M. Killinger, Ph.D. (Stauffer Chemical Company) containing Dr. Scott's review of the mouse teratology study.

2. A statement indicating that on December 9, 1981, EPA informed Stauffer that the 3-generation reproduction study in rats was acceptable as the first of the two required teratology studies on dyfonate. There should, therefore, be no data gap for a second species teratology study.

3. A request to change the submission date for the final report of the new chronic feeding/oncogenicity study on rats from March 31, 1987 to June, 1989.

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Response:

1. Mouse Teratology Study

Based, in part, on the additional information and comments from Stauffer Chemical Company on the mouse teratology study, Toxicology Branch (TB) has concluded the following.

(a) The sternebral malalignment and slight dilation of the 4th cerebral ventricles observed in this study are, most likely, not frank malformations (i.e., are not terata) but, rather, are manifestations of fetotoxicity. These lesions most probably indicate developmental variants or delayed developmental processes of minor morphologic significance.

(b) Most of these lesions occurred at or very near maternally toxic dosage levels. Due to the incidence patterns, it is most difficult to assign a definitive NOEL to these effects. The NOEL is probably about 2 mg/kg/day (the lowest dosage level).

(c) This study is classified as Core Minimum. Although some slight uncertainty exists regarding the NOEL for fetotoxicity, this is considered to be of insufficient concern at this time to warrant requiring the study to be repeated. No teratogenic effect due to the test material was observed in this study at dosage levels up to and including 8 mg/kg/day (the highest dosage level). The maternally toxic NOEL is 6 mg/kg/day and the maternally toxic LOEL is 8 mg/kg/day.

2. Neither TB nor PM Team #16 in Registration Division (RD) is aware of or has been able to locate the December 9, 1981 letter referred to by Stauffer. Stauffer should be asked to provide EPA with a copy of the letter. Also, the 3-generation reproduction study in rats (Woodard Research Corp., dated January 10, 1969; MRID #00082234) has been misplaced in TB and can not be found at this time. TB requests RD to obtain another copy of this study and submit it to TB for review for the purpose of determining whether or not it contains an acceptable teratology study incorporated into it. In the interim, the data gap for a second species teratology study should remain.

3. Change in Submission Date

TB has no objection to changing the submission date for the final report of the new chronic feeding/oncogenicity study on rats from March 31, 1987 to June, 1989.

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