



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

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

OCT 28 1991

MEMORANDUM

SUBJECT: REVIEW OF ADDITIONAL INFORMATION ON A MONKEY
DERMAL PHARMACOKINETIC STUDY SUBMITTED IN SUPPORT OF
THE ESTIMATION OF APPLICATOR EXPOSURE FROM DITHIOPYR

TO: Ms. Joanne I. Miller, PM 23
Fungicide-Herbicide Branch
Registration Division (H7505C)

FROM: Arthur O. Schlosser, Chemist *Arthur O. Schlosser*
Special Review and Registration Section
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

THRU: Curt Lunchick, Head *Curt Lunchick*
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Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

Please find below the OREB review of.....

HED Project #: 1-2280

Reg File/Rec #: _____

Registration #: 524-430 and 431

Caswell #: 717C

Company Name: Monsanto

Date Received: 9/13/91

Action Code: 575

Monitoring Study Requested: _____

Reviewing Time: 1 day

INTRODUCTION

Registration Division (RD) has requested that OREB review and comment on additional information concerning a monkey dermal pharmacokinetic study submitted by the registrant (Monsanto) in support of an estimation of applicator exposure to dithiopyr.

CONCLUSIONS/RECOMMENDATIONS

OREB has been in contact with Dr. Chin (Tox Branch I) and has been informed that he agrees with Monsanto's arguments that the skin penetration data in question should not be required. A meeting with Monsanto is, therefore, unnecessary. Dr. Chin will respond to RD in a separate memo.

It is noted that in the OREB (Versar) review of exposure studies for use of dithiopyr on turf (Final Report March 6, 1991) several deficiencies were identified. These should be addressed by the registrant.

DISCUSSION

The registrant, in a letter of 27 August 1991, states that a monkey dermal pharmacokinetics study previously submitted in support of a dithiopyr applicator biomonitoring study was mistakenly assumed to have been a dermal penetration study and was found to be deficient as such in toxicology review. When dithiopyr (Dimension Turf Herbicide) was registered on 18 June 1991, a dermal penetration study was listed as a condition of registration. The registrant further claims that dithiopyr does not have the toxicity profile which would reasonably lead to a requirement for a formal Dermal Penetration study under Toxicology guidelines (Guidelines 85-2) and that the study submitted is adequate for the purpose for which it was submitted.

The biomonitoring study supported by the monkey pharmacokinetics study has been used by OREB to make an applicator exposure assessment (C. Lunchick, HED Project #1-0040, 4 Feb 1991). OREB's contractor Versar participated in the review of the study. Certain deficiencies in the study were identified in the Versar final report of March 6, 1991.

Monsanto has requested that OREB be in contact with the Toxicology reviewer for dithiopyr and try to resolve jointly the matter of the acceptability of the monkey pharmacokinetics study. They suggested that a meeting between Monsanto and HED staff be arranged if necessary.

The OREB reviewer has been in contact with Dr. Paul Chin of Tox Branch I (identified as the Tox reviewer of dithiopyr). In a

telephone communication with Dr. Chin on October 22, 1991, Dr. Chin stated that he agreed with Monsanto's contentions that a skin penetration study would not be required and that a meeting with Monsanto would not be necessary. Dr. Chin will respond to RD on this matter in a separate memo (bean).

cc: A. Schlosser OREB/HED (H7509C)
P. Chin TOX/HED (H7509C)
Chemical file/dithiopyr
Correspondence
Circulation