Shaughnessy No.: 060101
Date Out of EFGWB: SEP 12 1991

To: Frank Rubis/Jay Ellenberger
Product Manager 50
Registration Division

From: A. Abramovitch, Ph.D., Chief
Environmental Chemistry Review Section #3
Environmental Fate and Ground Water Branch/EFED

Through: Henry Jacoby, Chief
Environmental Fate and Ground Water Branch/EFED

Attached, please find the EFGWB review of . . .

Reg./File # : Reregeistration case 2670, DP BARCODE 166072

Common Name : Thiabendazole

Type Product : Fungicide

Product Name : TBZ

Company Name : Merck and Company, Inc.

Purpose : Phase IV reregistration

Date Received: 7/10/91 EFGWB # (s): 910723

Action Code :

Deferrals to:

_____ Ecological Effects Branch, EFED

_____ Science Integration and Policy Staff, EFED

_____ Non-Dietary Exposure Branch, HED

_____ Dietary Exposure Branch, HED

_____ Toxicology Branch I, HED

_____ Toxicology Branch II, HED

1. CHEMICAL: Common name:

Thiabendazole.

Chemical name:

2-(thiazol-4-yl)benzimidazole;
2-(1,3-thiazol-4-yl)benzimidazole.

Trade name(s):

Arbotect, Mertect, TBZ, Tecto, Thibenzole.

Formulations:

WP (40, 60, 90%); FC.

Physical/Chemical properties:

Molecular formula: $C_{10}H_7N_3S$.
Molecular weight: 201.1.
Physical state: Powder.
Vapor pressure: $4x10^{-9}$
Solubility: At 25 C: c. 10g/L in water at pH 2; <50 mg/L in water at pH 5-12; >50 g/L at pH 12; 4.2 g/L acetone; 7.9 g/L ethanol; 2.1 g/L ethyl acetate. At "room temperature": 230 mg/L benzene; 80 mg/L chloroform; 39 g/L dimethylformamide; 80 g/L dimethyl sulfoxide; 9.3 g/L methanol.

2. TEST MATERIAL: N/A

3. STUDY/ACTION TYPE:

12 months extension request to conduct the confined crop rotation study.

4. STUDY IDENTIFICATION: Confined crop rotation study.

5. REVIEWED BY:

Akiva D. Abramovitch, Ph.D., Chief
Section 3, EFGWB/EFED

Signature: Akiva Abramovitch
Date: SEP 10 1991

6. CONCLUSION:

EFGWB accepts the explanation provided by the registrant for the delay in completing the confined crop rotation study on thiabendazole. Therefore, EFGWB concurs with granting the registrant a one year extension to July 12, 1992 to submit the study.

7. RECOMMENDATION:

The registrant should proceed to fulfill the data requirements listed as unsatisfied in the Phase IV review of February 8, 1991.

8. BACKGROUND:

A. Introduction- see Phase IV review of Feb. 8, 1991.

B. Direction for Use- Not specified.

9.0 DISCUSSION OF INDIVIDUAL STUDIES: N/A

10.0 COMPLETION OF ONE-LINER: not applicable.

11.0 CBI APPENDIX: None.

EFGB Rm 1016

DP BARCODE: D166072 REREG CASE # 2670

CASE: 818982 DATA PACKAGE RECORD DATE: 07/09/91
SUBMISSION: S398805 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REREGISTRATION ACTION: 610 TIME EXTENTION REQUEST
CHEMICALS: 060101 Thiabendazole

ID#: 060101
COMPANY:
PRODUCT MANAGER: 51 BARBARA BRISCOE 703-308-8065 ROOM: CS1 3H3
PM TEAM REVIEWER: FRANKLIN RUBIS 703-308-8184 ROOM: CS1 4J6
RECEIVED DATE: 06/18/91 DUE OUT DATE: 08/27/91

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 166072 EXPEDITE: N DATE SENT: 07/09/91 DATE RET.: / /
CHEMICAL: 060101 Thiabendazole
DP TYPE: 999 Miscellaneous Data Package
ADMIN DUE DATE: 08/28/91 CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT
DIV : EFED	07/10/91	/ /
BRAN: EFGB	/ /	/ /
SECT: IO	/ /	/ /
REVR :	/ /	/ /
CONTR:	/ /	/ /

* * * DATA REVIEW INSTRUCTIONS * * *

The 5/22/91 letter requests a 1-year time extension for GRN 165-1. Your comments are requested.

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL

MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
HILLSBOROUGH ROAD, THREE BRIDGES, NEW JERSEY 08887

PATRICIA A. SAMUEL
MANAGER, REGULATORY AFFAIRS
AGRICULTURAL RESEARCH & DEVELOPMENT

(908) 369-3072

May 22, 1991

Mr. Jay Ellenberger
Office of Pesticide Programs
Document Processing Desk (DCI Thiabendazole)
Special Review & Reregistration
Division - H7505C
Generic Chemical Support Branch
ENVIRONMENTAL PROTECTION AGENCY
Crystal Mall #2
1921 Jefferson Davis Highway
Arlington, VA 22202

Dear Mr. Ellenberger:

Thiabendazole: Comprehensive Data Call-In
Request for Extension: GRN 165-1 Confined Rotational Crop Study

In our letter of 8/15/88, we committed to conduct a Confined Rotational Crop Study with thiabendazole to fulfill GRN 165-1 requirements in response to EPA's 3/24/88 Comprehensive Data Call-In. The study was contracted to ABC Laboratories, Inc., Columbia, Missouri, and initiated April, 1989. ABC Laboratories, Inc. were also contracted to perform three plant and two animal metabolism studies.

As indicated in our progress reports for ongoing thiabendazole studies, samples from the Confined Rotational Crop Study were analyzed only for total residues, until the completion of the Residue Chemistry: Plant Metabolism Studies (GRN: 171-4). Problems encountered with the three plant metabolism studies were associated with difficulties in extracting radioactive residues and the isolation and characterization of unidentified metabolites. Likewise, similar difficulties were also encountered in the ongoing animal metabolism study. Submission of the plant metabolism reports was extended to May 1991. The final reports were submitted to the Agency on 5/7/91.

Although the schedule was tight, we fully expected to meet the Confined Rotational Crop July 1991 submission date. Administrative and technical delays at ABC Laboratories, arising from staff turnover and shortages, and technically demanding and ongoing animal metabolism studies (poultry and goat), have adversely impacted on our ability to meet the current deadline. Continued work was deferred on the rotational crop studies. The difficulties associated with the plant and animal metabolism studies delayed the transfer of the technology and information gained from those studies to the crop rotation study. It is therefore planned that upon

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completion of the animal metabolism reports (due for submission 9/1/91) additional manpower will be assigned to the crop rotation study. Using the information gained from the earlier studies, the radioactive residues found in the rotational crops at significant levels will be identified or characterized.

Merck is committed to fulfilling our obligations to the reregistration requirements in an adequate and timely manner; however, we have no choice but to request a 12-month extension to July, 1992 in order to allow completion of the rotational crop study by ABC Laboratories and reporting of the results to the Agency.

The nature of the problems, and commitment from ABC Laboratories to expedite completion of the study as soon as possible are outlined in the attached letter of May 22, 1991 from Dr. Timothy Halls, ABC Laboratories. We regret being unable to fulfill our commitment for this required study in a timely manner. We fully intend to honor our commitment to conduct and report an acceptable study but as indicated we will require a 12-month extension to July 1992 to meet this obligation.

Should there be questions regarding this matter, please contact me at the letterhead address or telephone number.

Sincerely,

Patricia A. Samuel

:cg

Attachment

cc: Ms. [redacted] - SRRD/EPA
Mr. Frank Rubis - SRRD/EPA
Dr. Richard A. Dybas - Merck & Co., Inc.
Dr. Samuel F. Rickard - Merck & Co., Inc.

ABC LABORATORIES

May 22, 1991

Ms. Patricia Samuel
Manager, Regulatory Affairs
Merck Sharp & Dohme Research Laboratories
Hillsborough Road
Three Bridges, NJ 08887

SUBJECT: Confined Rotational Crop Study Involving Thiabendazole

Dear Ms. Samuel:

As we recently discussed, the confined rotational crops study involving thiabendazole being performed here at ABC Laboratories cannot be completed in time for submission prior to the July 1991 deadline. The reasons for this delay are related to various problems, including key staff departures, recruitment of additional personnel, and difficulties associated with extraction and chromatographic methods; all of which impeded an earlier completion of the recently-submitted plant metabolism studies (wheat, soybean and sugar beets). Furthermore, intensive work on the ongoing animal metabolism studies is also impeding progress on the rotational crop study.

Specifically, in these plant metabolism studies, there were delays associated with difficulties in a quantitative extraction of incurred radioactive residues from various plant matrices, especially the mature tissues. In addition, some unextractable and/or unidentified residues could not be readily characterized because method development took a longer time than anticipated. These problems were compounded by the departure of some key personnel, including the then Study Director. Eventually, these technical and personnel-related issues were resolved and the reports have since been submitted to Merck & Co.

Based on the constraints outlined above, the technical expertise acquired from the plant metabolism studies have yet to be transferred to the rotational crop study. Work on the rotational crop study was deferred during completion of the plant metabolism work (and completion method development in plants). Progress on the rotational crop study, therefore, has been limited to total residue analysis in all samples and a small amount of extraction/characterization. From the just-completed plant metabolism studies, we now know the identity of the residues for which to look in the various rotational crop matrices.

However, the number of personnel available, the technical demands of the ongoing animal metabolism studies (poultry and goat), and the close deadline for those animal metabolism studies factor into our lack of ability to make rapid progress on the rotational crop study. As

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7200 E. ABC Lane ▪ P.O. Box 1097 ▪ Columbia, MO 65205 ▪ 314-474-8579 ▪ FAX 314-443-9033

with the plant metabolism work, interim loss of study directors impeded progress on the animal studies. Further, we are experiencing continuing difficulties associated with the characterization and chromatographic optimization of some incurred polar metabolites. Therefore, only after the completion of the animal metabolism studies and reports will sufficient resources be available to complete the rotational crop study. As a result of these time and personnel constraints, we will need a significant time extension beyond the July 1991 submission deadline for the rotational crop study.

Completion of the animal metabolism studies will permit more manpower to be applied to the crop rotational study. For that study, additional laboratory work will be needed to complete the extractions, cleanups and chromatographic profiling for the various plant matrices, including the mature tissues. Beyond these laboratory phases, additional time will be needed for assembly of the massive data package, report writing and reviews, and final quality assurance audits by both ABC Laboratories' and Merck's QA Units.

Please rest assured that we at ABC will do our very best to expedite a successful completion of this study in the least possible time and to cooperate with Merck & Co. in satisfying any concerns the EPA may have regarding this deadline issue.

Sincerely,

Timothy D.J. Halls, Ph.D.
Vice President
Metabolism Programs