

(UN DATED)

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Shaughnessy No.: 060101

Date Out of EFGWB: _____

To: Product Manager
Registration Division (H-7505C)

From: Akiva Abramovitch, Chief
Environmental Chemistry Review Section #3
Environmental Fate and Ground Water Branch/EFED (H-7507C)

Through: Henry Jacoby, Chief
Environmental Fate and Ground Water Branch/EFED (H-7507C)

Attached, please find the EFGWB review of . . .

Reg./File # : 148-79-8.

Common Name : Thiabendazole.

Type Product : Fungicide.

Product Name : Arbotect, Mertect, TBZ, Apl-Luster, Bioguard, Bovizole, Epro-
fil, Equizole, Lombristop, Mertect 160, Metasol TK 100,
Mintesol, Mycozol, MK 360, Nemapan, Omnizole, Polival, Tebu-
zate, Tecto, Thibenzole 200, Thiprazole, Top form wormer, and
Agrosol.

Company Name : Merck & Company, Inc.

Purpose : Review of an accumulation in confined rotational crops study.

Date Received: _____ EFGWB # (s): _____

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.

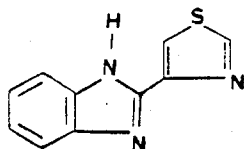
Chemical name:

2-(4'Thiazolyl)benzimidazole.

Trade name(s):

Arbotect, Mertect, TBZ, Apl-Luster, Bioguard, Bovizole, Eprofil, Equizole, Lombristop, Mertect 160, Metasol TK 100, Mintesol, Mycozol, MK 360, Nemapan, Omnizole, Polival, Tebuzate, Tecto, Thibenzole 200, Thiprazole, Top form wormer, and Agrosol.

Structure:



Formulations:

Wettable powder, flowable concentrate, and dust.

Physical/Chemical properties:

Molecular formula: C₁₀H₇N₃S.
Molecular weight: 201.1.
Physical state: Colorless powder.
Melting point: 304-305 C.
Solubility (25 C): c. 10 g/L water (pH 2); <50 mg/L water (pH 5-12); >50 g/L water (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:

Study 1: Active ingredient.

3. STUDY/ACTION TYPE:

Review of an accumulation in confined rotational crops study.

4. STUDY IDENTIFICATION:

Halls, T.D., and D.R. Sanson. 1992. "C-Thiabendazole - Confined accumulation on rotational crops. Laboratory Report No. 37727. Unpublished study performed by ABC Laboratories, Inc., Columbia, MO, and submitted by Merck & Company, Inc., Rahway, NJ. (42367801)

5. REVIEWED BY:

James A. Breithaupt
Agronomist
EFGWB/EFED/OPP
Review Section #3

Signature: _____

Date: _____

6. APPROVED BY:

Akiva D. Abramovitch
Chief
EFGWB/EFED/OPP
Review Section #3

Signature: _____

Date: _____

7. CONCLUSION:

8. RECOMMENDATIONS:

9. BACKGROUND:

A. Introduction

B. Directions for Use

Thiabendazole is a systemic fungicide registered for use on a wide variety of terrestrial food crop (citrus, bananas, apples, pears, and sweet potatoes) and terrestrial non-food crop (ornamentals, turf, and tobacco) sites. Applications may be made during the growing season to control pathogenic fungi and post-harvest to control storage diseases. Single active ingredient formulations include wettable powder, flowable concentrate, and dust. Multiple active ingredient formulations include captan, thiram, quintozone, and prochloraz. Thiabendazole is nontoxic to bees and slightly toxic to fish.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

Refer to attached reviews.

11. COMPLETION OF ONE-LINER:

12. CBI APPENDIX:

All data reviewed here are considered "company confidential" by the registrant and must be treated as such.

THIABENDAZOLE

TASK 1: REVIEW AND EVALUATION OF INDIVIDUAL STUDIES

October 12, 1992

Initial Draft Report

Contract No. 68D20057

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3262

THIABENDAZOLE

Table of Contents

	<u>Page</u>
Introduction	
Scientific Studies	
1. Accumulation in confined rotational crops. (Halls and Sanson, 42367801)	1.1
References	2.1
Appendix	2.2

INTRODUCTION

Thiabendazole is a systemic fungicide registered for use on a wide variety of terrestrial food crop (citrus, bananas, apples, pears, and sweet potatoes) and terrestrial non-food crop (ornamentals, turf, and tobacco) sites. Applications may be made during the growing season to control pathogenic fungi and post-harvest to control storage diseases. Single active ingredient formulations include wettable powder, flowable concentrate, and dust. Multiple active ingredient formulations include captan, thiram, quitozene, and prochloraz. Thiabendazole is nontoxic to bees and slightly toxic to fish.

DATA EVALUATION RECORD

DRAFT

STUDY 1

CHEM 060101 Thiabendazole \$165-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 42367801
Halls, T.D., and D.R. Sanson. 1992. ¹⁴C-Thiabendazole - Confined
accumulation on rotational crops. Laboratory Report No. 37727.
Unpublished study performed by ABC Laboratories, Inc., Columbia, MO, and
submitted by Merck & Company, Inc., Rahway, NJ.

DIRECT REVIEW TIME = 36

REVIEWED BY: M. Dillman TITLE: Staff Scientist

EDITED BY: W. Martin TITLE: Staff Scientist
J. Harlin Staff Scientist

APPROVED BY: W. Spangler TITLE: Project Manager

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Rockville, MD
TEL: 301-417-9800

APPROVED BY: J. Breithaupt
TITLE: Agronomist
ORG: EFGWB/EFED/OPP
TEL: 703-305-5925

SIGNATURE:

DRAFT

CONCLUSIONS:

Confined Accumulation - Rotational Crops

1. This study cannot be used to fulfill data requirements at this time.
2. These data are of uncertain value and should not be used to predict the environmental behavior of thiabendazole and its degradates.
3. This study is unacceptable at this time for the following reason:

it was not possible to reproduce the reported concentrations of thiabendazole residues from the raw data provided.



9

In addition, this study does not fulfill Subdivision N guidelines for the following reasons:

radioactivity present in the plant extracts at up to 4.0 ppm was not identified, and

radioactivity present in the aqueous soil extracts at up to 0.1779 ppm and in the organic soil extracts at up to 0.1420 ppm was not identified.

4. In order for this study to be re-evaluated for fulfillment of data requirements, the registrant must provide detailed explanations for the calculation of thiabendazole residue concentrations. Additionally, the registrant must characterize all of the radioactivity in the plant and soil extracts and identify any degradates present at ≥ 0.01 ppm.

METHODOLOGY:

The test site (30 x 60 feet) was surrounded by fencing and covered with a corrugated fiberglass roof. During the winter, the test site was enclosed in polyethylene sheeting and heated by gas heaters. Within this shelter, five test plots (3 x 8 x 2 feet) were created by burying fiberglass-coated tanks to a depth of 18 inches, and filling them with sandy loam soil (70% sand, 20% silt, 10% clay, pH 8.0, CEC 8.6 meq/100 g, organic matter content not reported) to within 6 inches of the top; plots were designated according to the rotational interval (30, 120, or 320 days posttreatment). Each plot was subdivided into three subplots; each subplot was planted to one of the three test crops (Figure 1). The plots apparently were planted to beans as a target crop.

Uniformly phenyl ring-labeled [¹⁴C]thiabendazole (TBZ; radiochemical purity 100%, specific activity 21,325 dpm/ug, MSDRL), dissolved in methanol, was applied twice at 0.96 lbs ai/A (total 1.92 lbs ai/A) with a carbon dioxide-sprayer to the 30- and 120-day rotational interval test plots on May 31, 1989, and June 15, 1989. A third plot (320-day plot) was treated once at 1.92 lbs ai/A on May 31, 1989. The two remaining plots, which served as controls, were covered with polyethylene sheeting during application of the test material.

At 30, 120, and 320 days posttreatment, one subplot in each of the treated and control plots was planted to lettuce, turnips, or wheat. Immature plant samples (26-52 days postplanting) were collected by thinning the crop, and mature samples (52-107 days postplanting) were collected by harvesting the remaining plants; randomly harvested plants were divided into triplicate subsamples. The entire aerial portion was harvested for all immature plant samples, mature lettuce, and mature wheat. The mature turnips were divided into aerial and root portions; the mature wheat was then divided into straw, hull, and grain portions. The plant samples were frozen (temperature not

specified) immediately after collection, and were stored for an unspecified time period; samples were then homogenized in dry ice and stored frozen at -20 C for an unspecified time period prior to analysis.

Soil samples were collected prior to treatment, 2 hours after the final treatment, and at all rotational crop planting and harvesting intervals; control plots were sampled before the treated plots. Single 12-inch soil cores were removed using a zero-contamination corer from all plots prior to treatment, and from control plots throughout the study; triplicate soil cores were removed from the treated plots at 2 hours post-final treatment, at planting, and at harvesting. Soil cores were frozen (temperature not specified) immediately after sampling for an unspecified time period. Prior to analysis, the soil cores were divided into 0- to 6- and 6- to 12-inch segments; segments from the same treatment interval, sampling interval, and soil depth were composited, homogenized, and stored at -20 C for an unspecified time period prior to analysis.

Subsamples of the soil were analyzed by LSC following combustion for total radioactive residue determination. Additional subsamples of the soil from the 2-hour and 30-day posttreatment sampling intervals were then acid-hydrolyzed with 6 N HCl:DMF (1:1, v:v; Figure 12). The slurries were shaken, centrifuged, and the supernatants were decanted. Soil samples were further rinsed with 6 N HCl:DMF (1:1) and then with water; the rinsates were combined with the supernatant. The combined supernatant was adjusted to pH 12 with NaOH, and extracted with ethyl acetate. Aliquots of the aqueous and ethyl acetate phases were analyzed by LSC. Additional aliquots of the ethyl acetate phase were analyzed by one-dimensional reverse-phase TLC on RP-18 plates eluted with water:acetonitrile:phosphoric acid (75:25:0.3, v:v:v); [¹⁴C]thiabendazole was applied to all plates as a reference standard. Radioactive areas were located by radioscanning. Subsamples of the extracted soils were analyzed by LSC following combustion.

The remaining soil samples were base-hydrolyzed with 3 N methanolic KOH (Figure 10). The slurries were refluxed overnight, centrifuged, and the supernatants were decanted. The methanol in the supernatant was removed under nitrogen; the residues were dissolved in water, and then extracted with ethyl acetate. The ethyl acetate was evaporated from the organic phase (method unspecified), and the residues were dissolved in methanol. Aliquots of the methanol solution were analyzed by LSC. The aqueous phase was acidified to pH 2, and aliquots were analyzed by LSC. The acidified aqueous phase was then lyophilized and the residues were redissolved in methanol; the solution was centrifuged and the supernatant was decanted. Aliquots of methanol solutions from both the aqueous and organic phases were analyzed by HPLC using a u-Bondapak C-18 column, eluted with a methanol and 0.1 M NaH₂PO₄/0.01 M NaClO₄ buffer gradient, with radioisotopic and UV (279 nm) detection; HPLC fractions were quantified by LSC. Radioactive peaks were identified by comparison

to retention times of reference standards (Figures 2 and 3) that were cochromatographed with the extracts. The solids remaining after the lyophilization of the aqueous phase were analyzed by LSC (preparation unspecified). Subsamples of the extracted soils were analyzed by LSC following combustion.

Subsamples of the plant tissues were analyzed by LSC following combustion for total radioactive residue determination. Plant samples were base-hydrolyzed with 3 N methanolic KOH (Figure 11). The mixtures were refluxed overnight, centrifuged, and the supernatants were decanted. The methanol in the supernatant was removed under nitrogen; the residues were dissolved in water, and then extracted with ethyl acetate. The ethyl acetate was evaporated from the organic phase (method unspecified), and the residues were redissolved in methanol. Aliquots of the methanol solution were analyzed by LSC. Additional aliquots were analyzed by HPLC using a u-Bondapak C-18 column eluted with a methanol and 0.1 M NaH_2PO_4 / 0.01 M NaClO_4 buffer gradient, with radioisotopic and UV (279 nm) detection; HPLC fractions were quantified by LSC. Radioactive peaks were identified by comparison to retention times of reference standards that were cochromatographed with the extracts. The aqueous phase was acidified to pH 2, then extracted again with ethyl acetate. Aliquots of the organic layer were analyzed by LSC and HPLC (as previously described). The remaining aqueous layer was lyophilized, the residues were redissolved in methanol, and the solution was centrifuged; aliquots of the supernatant were analyzed by HPLC (as previously described). The undissolved solids remaining after the lyophilization of the aqueous phase were analyzed by LSC (preparation unspecified). Selected HPLC eluent fractions were further analyzed by one-dimensional reverse-phase TLC as previously described and/or GC/MS for confirmation of degradate identifications.

DATA SUMMARY:

[^{14}C]Thiabendazole residues accumulated in lettuce, turnips, and wheat planted 30 and 120 days after sandy loam soil was treated twice at 0.96 lbs ai/A (total 1.92 lbs ai/A), and 320 days after sandy loam soil was treated once at 1.92 lbs ai/A with uniformly phenyl ring-labeled [^{14}C]thiabendazole (TBZ; radiochemical purity 100%). Thiabendazole was 0.0464-0.2900 ppm in the lettuce samples, 0.0416-0.4161 ppm in the turnip samples, and 0.0106-2.5518 ppm in the wheat samples (Tables XII and XIV). In the upper 6 inches of soil, thiabendazole was 0.5111-0.9537 ppm, with no discernible pattern (Tables VI, VIII and X).

The degradate identified in both the plant substrates and the soil was

free benzimidazole (BNZ).

The degradates identified only in the plant substrates were:

sugar-bound benzimidazole conjugate(s) (BNZ-GLU); and
5-hydroxythiabendazole (5-OH-TBZ).

In immature lettuce, total radioactive residues were 0.3680 ppm in the samples from the 30-day rotational interval, 0.6638 ppm from the 120-day interval, and 1.5592 ppm in the crop from the 320-day rotational interval (Tables XI and XII). Thiabendazole was 0.0707 ppm in the samples from the 30-day rotational interval, 0.2317 ppm in the 120-day crop, and 0.2900 ppm in the 320-day crop. Free benzimidazole was <0.005-0.0053 ppm; benzimidazole conjugates were 0.0467 ppm in the 30-day crop, 0.1381 ppm in the 120-day crop, and 0.8077 ppm in the 320-day crop; and 5-hydroxythiabendazole was 0.04-0.10 ppm (0.10 ppm in the 320-day crop; Residue Summary Table and Tables XI and XII). Unidentified extracted radioactivity comprised 0.1484-0.2040 ppm (reviewer calculated), and unextracted radioactivity was 0.0471-0.1575 ppm (10.1-13.6% of the total recovered residues).

In mature lettuce, total radioactive residues were 0.2744-0.6579 ppm, with no discernible pattern; the maximum total radioactivity was observed in the 30-day crop (Tables XI and XII). Thiabendazole was 0.2270 ppm in the samples from the 30-day rotational interval, 0.0464 ppm in the 120-day crop, and 0.0791 ppm in the 320-day crop. Free benzimidazole was <0.005-0.0097 ppm, benzimidazole conjugates increased from 0.0322 ppm to 0.3128 ppm, and 5-hydroxythiabendazole was <0.005 in the 30-day crop and 0.04 ppm in the 120- and 320-day crops (Residue Summary Table and Tables XI and XII). Unidentified extracted radioactivity was 0.0477-0.2783 ppm (reviewer calculated); unextracted radioactivity was 0.0102-0.1204 ppm (3.7-18.3% of the total residues).

In immature turnip tops, total radioactive residues were 0.0952-0.8491 ppm, with no discernible pattern; the maximum total radioactivity was observed in the 120-day crop (Tables XI and XII). Thiabendazole was 0.0416-0.4161 ppm, free benzimidazole was <0.005-0.0866 ppm, and benzimidazole conjugates were 0.0225-0.1299 ppm; the maximum concentrations of all degradates were in the 120-day crop. The degradate 5-hydroxythiabendazole was not detected in samples from any rotational interval (Residue Summary Table). Unidentified extracted radioactivity was 0.0227-0.1732 ppm (reviewer calculated) and unextracted radioactivity was 0.0084-0.0433 ppm (5.1-10.3% of the total residues); the maximum concentrations were in the 120-day crop.

In mature turnip tops, total radioactive residues were 0.6346 ppm in the 30-day crop samples, 0.7749 ppm in the 120-day crop, and 1.0542 ppm in the 320-day crop (Tables XI and XII). Thiabendazole was 0.1107-0.3193 ppm, with no discernible pattern; free benzimidazole was 0.0267 ppm in the 30-day crop and \leq 0.0084 ppm in the 120- and 320-day crops, benzimidazole conjugates were 0.0504-0.0558 ppm in the

30- and 120-day crops and 0.4175 ppm in the 320-day crop, and 5-hydroxythiabendazole was <0.005-0.05 ppm (Residue Summary Table and Tables XI and XII). Unidentified extracted radioactivity was 0.2570-0.4107 ppm (reviewer calculated); unextracted radioactivity was 0.0488-0.0736 ppm (5.4-11.6% of the total residues).

In mature turnip roots, total radioactive residues were 0.1464-0.1627 ppm (Tables XI and XII). Thiabendazole increased from 0.0758 ppm in the 30-day crop to 0.1106 ppm in the 320-day crop. Benzimidazole conjugates were <0.005-0.0142 ppm. The degradates free benzimidazole and 5-hydroxythiabendazole were not detected. Uncharacterized extracted radioactivity was 0.017-0.0517 ppm (reviewer calculated); unextracted radioactivity was 0.0122-0.0192 ppm (8.2-12.9% of the total residues).

In immature wheat forage, total radioactive residues were 0.5646-2.2918 ppm, with no discernible pattern; the maximum total radioactivity was observed in the 120-day plot (Tables XIII and XIV). Thiabendazole was 0.1259-0.6577 ppm, free benzimidazole was <0.005-0.1879 ppm, benzimidazole conjugates were 0.0683-0.2956 ppm, and 5-hydroxythiabendazole was 0.03-0.18 ppm; the maximum concentrations of all degradates were in the 120-day crop (Residue Summary Table and Tables XIII and XIV). Uncharacterized extracted radioactivity was 0.1899-0.7231 ppm (reviewer calculated); unextracted radioactivity was 0.1061-0.2475 ppm (9.3-18.8% of the total residues); the maximum concentrations were observed in the 120-day crop.

In mature wheat straw, total radioactive residues were 2.6069-10.2483 ppm, with no discernible pattern (Tables XIII and XIV). Thiabendazole was 0.8863-2.5518 ppm, free benzimidazole was 0.0182-0.7686 ppm, benzimidazole conjugates were 0.7795-1.7217 ppm, and 5-hydroxythiabendazole was <0.005-0.70 ppm; the maximum concentrations of degradates were observed in the 320-day crop (Residue Summary Table and Tables XIII and XIV). Uncharacterized extracted radioactivity was 0.8942-4.0143 ppm (reviewer calculated); unextracted radioactivity was 0.0287-0.4919 ppm (1.0-4.8% of the total residues); the maximum concentrations were in the 320-day crop.

In mature wheat hulls, total radioactive residues were 1.1314-6.5780 ppm, with no discernible pattern (Tables XIII and XIV). Thiabendazole was 0.6358-2.4181 ppm, free benzimidazole was <0.005-0.8486 ppm, benzimidazole conjugates were 0.0057-1.0196 ppm, and 5-hydroxythiabendazole was <0.005-0.01 ppm (Residue Summary Table and Tables XIII and XIV). Unidentified extracted radioactivity was 0.4084-2.5554 ppm (reviewer calculated); unextracted radioactivity was <0.005-0.1381 ppm (up to 7.2% of the total residues).

In mature wheat grain, total radioactive residues were 0.0530-0.1814 ppm, with no discernible pattern (Tables XIII and XIV). Thiabendazole was 0.0106-0.0856 ppm, benzimidazole conjugates were <0.005-0.0238 ppm, and 5-hydroxythiabendazole was <0.005-0.01 ppm; maximum concentrations of all degradates were in the 320-day crop

(Residue Summary Table and Tables XIII and XIV). The degradate free benzimidazole was not detected. Unidentified extracted radioactivity was 0.0177-0.0387 ppm (reviewer calculated); unextracted radioactivity was <0.005-0.0443 ppm (up to 24.4% of the total residues).

In the upper 6 inches of the soil of the treated plots, the total radioactive residues were 0.6418-1.1490 ppm throughout the study, and thiabendazole was 0.5111-0.9527 ppm, with no discernible pattern.

In the 0- to 6-inch soil depth, total residues in the plot planted at 30 days posttreatment were 0.6418-0.9773 ppm with no discernible pattern; the maximum total residues were observed at 137 days posttreatment (Table VI). Thiabendazole was 0.6084-0.7375 ppm; and free benzimidazole was 0.0422 and 0.0058 ppm at 75 and 95 days posttreatment, respectively. Uncharacterized radioactivity in the organic extracts was 0.0276-0.0557 ppm (reviewer calculated), and uncharacterized radioactivity in the aqueous extract was present at up to 0.1779 ppm. Unextracted radioactivity comprised up to 0.1210 ppm (14.5% of total recovered residues). In the 120-day plot, total residues were 0.6883-1.1490 ppm; maximum total residues were observed at 153 days posttreatment (Table VIII). Thiabendazole was 0.5176-0.9537 ppm and free benzimidazole was 0.0596 ppm at 120 days posttreatment. Uncharacterized radioactivity in the organic extracts was 0.0129-0.0676 ppm (reviewer calculated), and uncharacterized radioactivity in the aqueous extract was present at up to 0.1677 ppm. Unextracted radioactivity comprised up to 0.1168 ppm (a maximum of 11.5% of total recovered residues). In the 320-day plot, total residues were 0.7441-0.9529 ppm; the maximum total residues were observed at 398 days posttreatment. Thiabendazole was 0.5111-0.8613 ppm and free benzimidazole was 0.0056 ppm at 372 days posttreatment (Table X). Uncharacterized radioactivity in the organic extracts was 0.0312-0.1420 ppm (reviewer calculated), and uncharacterized radioactivity in the aqueous extract was present at up to 0.1570 ppm. Unextracted radioactivity comprised up to 0.1182 ppm (12.4% of total recovered residues).

In the 6- to 12-inch soil depth, total residues were 0.0379, 0.1057, and 0.0369 ppm at 56, 75, and 137 days posttreatment, respectively, in the plot for the 30-day rotational interval. At 75 days posttreatment (only sample analyzed by HPLC), thiabendazole was 0.0635 ppm, radioactivity in the aqueous extract was 0.0157 ppm, and unextracted radioactivity was 0.0234 ppm (22.1% of recovered radioactivity; Table VI). In the 120-day plot, total residues were <0.005-0.0989 ppm with no discernible pattern, the maximum concentration was at 223 days posttreatment. At 223 days posttreatment (only sample analyzed by HPLC), thiabendazole was 0.0782 ppm, radioactivity in the aqueous extract was 0.0104 ppm, and unextracted radioactivity was 0.0103 ppm (10.4%; Table VIII). In the 320-day plot, total residues were 0.0484 and 0.0254 ppm at 320 and 372 days posttreatment, respectively; the samples were not analyzed by HPLC (Table X).

COMMENTS:

1. The Dynamac reviewer could not reproduce the reported concentrations of thiabendazole residues from the HPLC raw data and total radioactive residues provided. Specifically, the reviewer was unable to consistently reproduce the reported thiabendazole and BNZ (free and conjugated) concentrations in the plant substrates based on the raw data provided from HPLC analyses. In addition, although 5-hydroxythiabendazole was reportedly identified through combinations of HPLC, TLC, and GC/MS analyses, examples of all analyses were not provided, and reported concentrations could not be reproduced from the HPLC raw data. The registrant must provide detailed explanations for these calculations and examples of all appropriate raw data.

This problem was compounded by the exclusion of the "tailing" before and after the thiabendazole peak in the HPLC radiochromatograms from the quantification of the parent compound. The study authors stated that including the tailing portions lead to inconsistencies in parent quantification from one sample to another. However, in chromatograms in which the radioactivity appeared to be exclusively parent compound, excluding the tailings significantly lowered the quantitation of parent. It was unclear to the reviewer whether the radioactivity attributed to tailing was quantitated.

Additionally, the distribution of radioactivity was normalized to the pre-extraction results for each sample matrix. Furthermore, all reported combustion results were corrected for matrix recoveries; thiabendazole matrix-specific recoveries ranged from 95.9 to 100%.

2. Radioactivity present at maximum concentrations ranging from 0.17 to 4.0143 ppm in extracts of immature lettuce, mature lettuce, immature turnips (tops), mature turnips (tops and roots), wheat forage, wheat straw, wheat hulls, and wheat grain were not characterized. Similarly, radioactivity in aqueous soil extracts at up to 0.25 ppm was not characterized. Subdivision N guidelines state that all degradates present at ≥ 0.01 ppm must be identified. According to the study authors, although unidentified radioactive residues were detected by HPLC in all plant matrices, none of the individual components was present "to levels of up to 0.005 ppm". No data were provided.

The study authors stated that the reported concentrations of parent thiabendazole and BNZ in plants were based on results from both organic-extractable fractions and, "if applicable," aqueous soluble fractions. However, the aqueous soluble fractions which were actually characterized have not been adequately specified. Since it was unclear which aqueous fractions were "applicable" when calculating the concentrations of uncharacterized radioactivity, the reviewer summed the amounts of radioactivity in the aqueous and organic extracts and subtracted the amounts of identified compounds from the total.

3. Adequate freezer storage stability data were not provided. According to the study authors, storage stability was investigated for "incurred" parent residues in wheat straw following freezer storage of two years; no decrease in radioactivity was observed. Furthermore, although total radioactivity did not decrease with time, the study authors did not discuss possible degradation during storage. Additionally, the temperature of the freezer storage was not specified for the stability study, the duration of freezer storage for the actual study samples was not specified, and no storage stability data were provided for the soil. The registrant must provide adequate storage stability data for the longest period of freezer storage for both plant and soil samples.
4. The test soil was incompletely characterized; the organic matter content was not reported. Subdivision N guidelines require that the test soil be completely characterized.
5. The study protocol indicated that navy beans were planted as a target crop at 30 days following the second treatment (July 15, 1989). Additionally, the protocol indicated that thiabendazole was to be applied at 10% bloom and peak bloom. The study authors did not address this discrepancy.
6. Polar metabolites (retention time = 3.5-6.0), which were observed in HPLC analyses of various plant substrates were reportedly indicative of the BNZ-sugar conjugates, as demonstrated in a wheat metabolism study (MRID 41872901, Laboratory Report No. 37724). Supporting data for the characterization of these peaks as BNZ conjugates and corresponding chemical structures were not provided with this study.
7. The 320-day test plot was inadvertently treated with the entire amount of thiabendazole (1.92 lbs ai/A) in one application, rather than in two separate applications (2 x 0.96 lbs ai/A). The study authors stated that it was unlikely that this deviation would have an impact on the outcome of the study since the plot was planted after approximately 1 year.
8. Fertilizers were applied to the soil throughout the study period. The following insecticides and fungicides were applied to control pest problems: disulfoton, propiconazole, dienochlor, diazinon, dicofol, abamectin, carbofuran, and Safer soap were applied to the wheat; lindane, Bacillus thuringiensis, and diazinon were applied to the lettuce; and Bacillus thuringiensis, Safer soap, and diazinon were applied to the turnips (Table XV). Weeding and crop-culturing were done manually, and no herbicides were applied during the study.
9. Air temperatures were recorded daily and soil temperatures were recorded twice daily. Irrigation data were also recorded; water volumes were calculated based on flow rate of the nozzle and time elapsed during watering. These data were not provided.

10. In Table III, the sampling intervals for mature and immature lettuce (357 days posttreatment) were identical in the 320-day plot; however, Tables XI and XII indicate that the immature lettuce was harvested at 357 days posttreatment, while the mature lettuce was harvested at 372 days. In addition, in the Residue Summary Table, the reported "total [¹⁴C] accounted for" of the 320-day mature turnip root crop (398 days posttreatment) is incorrect, and should be 87%.
11. The study authors stated that a portion of the raw data dealing with the precise determination of the application rate could not be located.
12. Unidentified extracted radioactivity from plant substrates was calculated by subtracting the unextracted radioactivity, free benzimidazole (BNZ), benzimidazole conjugate(s) (BNZ-GLU), and 5-hydroxythiabendazole (5-OH-TBZ) from the total radioactive residues (TRR; Residue Summary Table and Tables XII and XIV).

Page _____ is not included in this copy.

Pages 19 through 52 are not included in this copy.

The material not included contains the following type of information:

- Identity of product inert ingredients.
- Identity of product impurities.
- Description of the product manufacturing process.
- Description of quality control procedures.
- Identity of the source of product ingredients.
- Sales or other commercial/financial information.
- A draft product label.
- The product confidential statement of formula.
- Information about a pending registration action.
- FIFRA registration data.
- The document is a duplicate of page(s) _____.
- The document is not responsive to the request.
- Internal deliberative information.
- Attorney-Client work product.
- Claimed Confidential by submitter upon submission to the Agency.

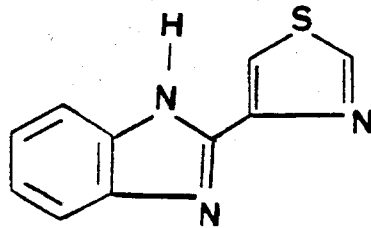
The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

REFERENCES

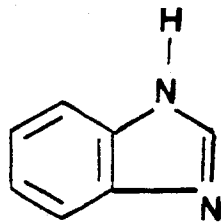
The following study was reviewed:

Halls, T.D., and D.R. Sanson. 1992. ¹⁴C-Thiabendazole - Confined accumulation on rotational crops. Laboratory Report No. 37727. Unpublished study performed by ABC Laboratories, Inc., Columbia, MO, and submitted by Merck & Company, Inc., Rahway, NJ. (42367801)

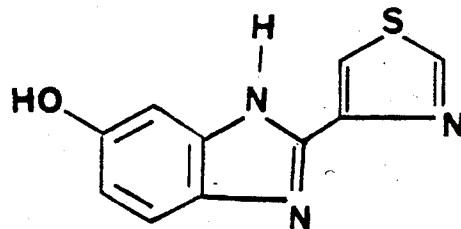
APPENDIX
THIABENDAZOLE AND ITS DEGRADATES



2-(4'-Thiazolyl)benzimidazole
(Thiabendazole)



Free benzimidazole (BNZ)



5-Hydroxythiabendazole (5-OH-TBZ)

