MRID 155575

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

5/5/86

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F3355 (RCB# 481). Thiabendazole (TBZ 060101-3) in or on Peanuts. Evaluation of Analytical Methods and Residue Data (Accession No. 261110).

FROM: Nancy Dodd, Chemist Nancy Dodd
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Ph.D., Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Henry Jacoby, PM #21
Fungicide-Herbicide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

Merck & Company, Inc. proposes tolerances for residues of the fungicide thiabendazole [2-(4-thiazolyl)-benzimidazole] in or on peanuts at 0.1 ppm and peanut hulls at 2.0 ppm.

Thiabendazole tolerances are established [40 CFR 180.242 and 21 CFR 561.380(a)] on a variety of commodities at levels ranging from 0.02 to 150 ppm. Tolerances are established for parent only except for animal commodities, which include parent and the metabolite 5-hydroxythiabendazole. Tolerances on animal commodities are 0.1 ppm for meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep; 0.1 ppm for eggs, and 0.4 ppm for milk.

No Registration Standard for thiabendazole has been issued.

Conclusions

1a. The proposed Section B/label should be revised by adding the statement "Apply by ground equipment only"; this mode of application is reflective of the residue data.

1b. The proposed Section B/label should be revised to prohibit grazing or feeding of peanut vines and hay since no tolerances have been proposed for these commodities.

1c. The proposed Section B/label should be revised to specify a maximum of seven applications.

1d. Pending RCB review of additional residue data which RCB now requests, a revised Section B/label may have to be submitted which proposes a PHI longer than 14 days (i.e. 28 days or longer). (see Residue section of this review for further details.)

2a. Parent thiabendazole, per se, is the residue of concern in peanuts.

2b. Thiabendazole and 5-hydroxythiabendazole are the residues of concern in animals.

3. Adequate analytical methods are available for enforcement of the established tolerances on peanuts, peanut hulls, and meat, milk, poultry, and eggs.

4. Adequate storage stability data are available.

5a. Additional residue data on peanuts and hulls, including PHI's of 14 days and longer than 28 days, are needed so that RCB can determine whether residues increase with time and, if so, when a plateau is reached (see Residue Data section of this review for further details).

5b. Fractionation studies show that residues apparently do not concentrate in crude oil, refined oil, or dried peanut meal.

5c. Residue data on the processed commodity soapstock should be provided.

6. RCB will reserve its conclusion on the adequacy of the established tolerances on meat, milk, poultry, and eggs resulting from the proposed use on peanuts until receiving residue data on peanut soapstock.

7. An International Residue Limits (IRL) Status Sheet is attached. A Codex proposal for thiabendazole on peanuts at 0.1 mg/kg is compatible with the U.S. proposed tolerance on peanuts. There are no Canadian or Mexican tolerances for thiabendazole on peanuts. Therefore, no compatibility questions exist with respect to Codex.

Recommendations

RCB recommends against this proposed use on peanuts for reasons given in Conclusions 1a, 1b, 1c, 1d, 5a, 5c, and 6 above.

Detailed Considerations

Manufacture

The synthesis of thiabendazole is summarized in the Merck Index. Technical thiabendazole contains 98.5% thiabendazole, traces of chlorinated thiabendazole, chlorinated aniline products, and aniline oxidation products. Toxicology Branch has concluded that the impurities are not likely to cause a residue problem (PP#6F1860, M. Bradley, September 19, 1977 and PP#2E2594, M. Bradley, February 8, 1982).

Formulation

Mertect 340-F (flowable/water dispersible suspension) contains 42% TBZ (3.8 lb ai/gal). The inerts have been cleared under 40 CFR 180.1001 for use on food crops (PP#2F2603, M. Bradley, February 8, 1982).

Proposed Use

Peanuts

Apply Mertect 340-F Fungicide to peanuts at the rate of 8 fl oz/A (0.24 lb ai/A) in sufficient water to obtain adequate coverage. Apply when leafspots caused by Cercospora arachidicola and Cereosporidium pernonatum first appear and repeat applications at 10 to 14 day intervals. Do not apply within 14 days of harvest. Mertect 340-F should be tank mixed with label rates of other registered fungicides to prevent further development of benzimidazole-tolerant strains.

RCB concludes that the proposed Section B/label should be revised by adding the statement "Apply by ground equipment only." (Refer to the Residue Data section.)

RCB also concludes that the proposed Section B/label should be revised to prohibit grazing or feeding of peanut vines and hay. (Refer to the Residue Data section.)

RCB also concludes that the proposed Section B/label should be revised to specify a maximum of 7 applications. (See Residue section of this review for further details.)

RCB also concludes that, pending RCB review of additional residue data which RCB now requests, a revised Section B/label may have to be submitted which proposes a PHI longer than 14 days (i.e. 28 days or longer). (See Residue section of this review for further details.)

Nature of the Residue

Plants

Thiabendazole is absorbed and translocated through the roots of cotton, soybean, pepper, and tomato seedlings but is not metabolized (PP#2E2594, M. Bradley, February 8, 1982).

The major portion of thiabendazole on bananas and citrus fruit remains on the peel although some transfer into the fruit occurs (PP#8F0674, W. Boodee, March 8, 1968).

Residues found on citrus a few weeks after treatment were conjugates of thiabendazole and 5-hydroxy-thiabendazole (up to 20%) and small amounts of 5-hydroxy-thiabendazole and related benzimidazoles. Toxicology Branch concluded that on citrus the tolerance could be expressed in terms of thiabendazole only. In other fruit (bananas and pome fruit), thiabendazole was the only residue of concern (PP#6F1860, M. Bradley, September 19, 1977).

RCB concludes that parent thiabendazole, per se, is the residue of concern in peanuts.

Animals

Metabolism in man was discussed in connection with PP#8F0674 (W. Boodee, March 8, 1968). TBZ is hydroxylated to 5-hydroxythiabendazole and then conjugated to form glucuronide and sulfate esters.

An article on metabolism in cows, goats, and swine (Tocco et al., "Absorption, Metabolism and Elimination of Thiabendazole

in Farm Animals and a Method for its Estimation in Biological Materials," J. of Pharmacology and Experimental Therapeutics, 149, pp. 263-271, 1965) has been reviewed in connection with PP#0G1001 (W. Cox, September 3, 1970). Residues in cows and goats were determined to be parent and 5-hydroxythiabendazole.

As stated in PP#5G3258 (L. Cheng, September 10, 1985), no conventional poultry metabolism study has been submitted. Since tolerances on animal commodities are already established, this deficiency will be addressed at the time a Registration Standard is done.

RCB concludes that thiabendazole and 5-hydroxythiabendazole are the residues of concern in animals.

Analytical Methods

Peanuts

The analytical method used to analyze peanuts is "Thiabendazole Determination in Peanuts." Peanut sample is extracted with ethyl acetate. The ethyl acetate extract is washed twice with NaOH. Then the ethyl acetate extract is washed with NaCl saturated water. The residue is extracted from the ethyl acetate with 0.1 N HCl. To the acid extract, 0.5 ml 2N NaOH, 2 ml 2N sodium acetate solution, 20 ml ethyl acetate, and 3 gms NaCl are added. After shaking, the ethyl acetate is collected. The residue is extracted from the ethyl acetate with 0.1 N HCl. Thiabendazole in 0.1 N HCl solution is determined spectrophotofluorometrically. Recoveries from peanuts fortified at 0.02 to 0.20 ppm were 62 to 105 percent. Controls were 0.004 to 0.017 ppm.

Peanut Hulls

The analytical method used to analyze peanut hulls is "Thiabendazole Determination in Wood Tissue and Peanut Hulls." Thiabendazole is extracted from milled peanut hulls by refluxing with acidified methanol. The methanol is evaporated. The thiabendazole is extracted from an aqueous solution of NaOH with ethyl acetate. The ethyl acetate extract is washed twice with 2N NaOH, and then with NaCl saturated water. The residue is extracted from the ethyl acetate with 0.1 N HCl. To the acid extract, 0.5 ml 2N NaOH, 3 ml 2N sodium acetate, 3 gms NaCl, and 20 ml ethyl acetate are added. After shaking, the ethyl acetate is collected. The residue is extracted from the ethyl acetate into 0.1 N HCl. TBZ in 0.1 N HCl solution is determined spectrophotofluorometrically. Recoveries from peanut hulls fortified at 0.10 to 2.0 ppm were 73 to 116 percent. Controls were 0.06 to 0.23 ppm.

Peanut Oil

The analytical method used to analyze peanut oil is "Thiabendazole Determination in Oil." Peanut oil is extracted with 0.1 N HCl. The sample is shaken with 2N NaOH in ethyl acetate to extract the residue into the ethyl acetate. The ethyl acetate is washed with NaCl saturated water. The residue is extracted with 0.1 N HCl. To the acid extract are added 0.5 ml 2N NaOH, 2 ml 2N sodium acetate solution, 20 ml ethyl acetate, and 3 gms NaCl. After shaking, the ethyl acetate is collected. The residue is extracted from the ethyl acetate with 0.1 N HCl. Thiabendazole in 0.1 N HCl is determined spectrophotofluorometrically. Recoveries from peanut oil fortified at 0.02 to 0.10 ppm ranged from 76 to 98 percent. Controls were 0.001 to 0.002 ppm.

Dried Peanut Meal

The analytical method used to analyze dried peanut meal is "Thiabendazole Determination in Dried Meal." The method is the same as described under "Peanuts." Recoveries from dried peanut meal fortified at 0.02 to 0.10 ppm were 51 to 53 percent. Controls were 0.001 ppm.

Meat, Milk, Poultry, and Eggs

Analytical methods are available for enforcement of the established tolerances for TBZ and 5-hydroxy-TBZ on meat and milk. Sensitivities of the methods were determined to be 0.05 ppm for milk and 0.1 ppm for meat in connection with PP#8F0724/FAP#8H2298 (B. Hopkins, August 23, 1968).

Analytical methods are available for enforcement of the established tolerances for TBZ and 5-hydroxy-TBZ on poultry and eggs. These methods are modifications of PAM II and Food Additives Analytical Methods (PP#6F1860, E. Leovey, August 6, 1979).

RCB concludes that adequate analytical methods are available for enforcement of the established tolerances on peanuts, peanut hulls, and meat, milk, poultry, and eggs.

Residue Data

Storage Stability

Storage stability data on sugar beet roots and tops were submitted with PP#2F1237 (E. Gunderson, July 31, 1972). Residues in sugar beet roots and tops which were stored frozen (-40 °F) for ca 7 months did not differ significantly from the original residue levels.

RCB concludes that adequate storage stability data are available.

Peanuts

Seven field studies were conducted in the states of AL, GA, NC, OK, TX, and VA. Mertect 340-F was applied at the rate of 8 fl oz/A (0.24 lb ai/A). Six to nine applications were made by ground equipment. Intervals between applications ranged from 5 to 22 days, but were mostly approximately 2 weeks apart. Preharvest intervals were 17 to 30 days except for a 1-day PHI in TX. Samples were shipped by air express to Rahway, NJ, where they were stored at 2 to 5 °C. Samples which were processed for analysis were processed within 2 to 3 days and placed in a freezer at -20 °F. Raw peanuts were sent by Federal Express to Texas for processing into oil and meal. After processing to oil and meal, the samples were frozen. Residues ranged from 0.00 to 0.07 ppm on peanuts and 0.12 to 1.68 ppm on hulls. Residues were $\leq$ 0.01 ppm on crude and refined oil and dried peanut meal processed from peanuts with residues of 0.03 ppm.

No residue data are available for aerial applications. Therefore, the proposed Section B/label should be revised by adding the statement "Apply by ground equipment only."

No residue data are available for peanut vines and hay. Therefore, the proposed Section B/label should be revised to prohibit grazing or feeding of peanut vines and hay.

Five of the seven studies carried out reflect seven applications. Therefore, the proposed Section B/label should be revised to specify a maximum of seven applications.

No residue data are available on peanut soapstock. Residue data for the processed commodity soapstock should be provided.

The proposed preharvest interval of 14 days is not supported by the residue data (PHI's of 1, 17, 18, 25, 28, and 30 days). The highest residue on peanuts (0.07 ppm) and hulls (1.68 ppm) occurred at a 28-day PHI, as shown in the following table:

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State	Rate (oz. product per A)	# of Applications	PHI	Thiabendazole Residue (ppm) Nuts	Hulls
Alabama	8	7	17	0.01	0.15-0.62
Georgia	8	7	18	0.00-0.01	0.12-0.22
North Carolina	8	9	18	0.02-0.04	0.66-1.02
Oklahoma I	8	7	25	0.04	0.88-1.02
Oklahoma II	8	7	28	0.01-0.07	0.44-1.68
Texas	8	7	1	0.02	0.80
Virginia	8	6	30	0.02-0.03	--

RCB cannot determine what residue levels were present in the Oklahoma II study at a 14-day PHI; it is predicted, however, to be higher than on day 28. None of the samples reflect a 14-day PHI. Only 1 sample reflects a PHI of less than 14 days (i.e. the 1-day PHI in the TX study). Also, the residue data seems to indicate that residues are increasing with increasing PHI's (excluding the Texas and Virginia studies). For these reasons, the petitioner should provide residue data for PHI's longer than 28 days so that RCB can determine whether residues increase with time and, if so, when a pleateau is reached.

RCB concludes the following:

a. A revised Section/B label should be submitted which adds the statement "Apply by ground equipment only."

b. A revised Section B/label should be submitted which prohibits grazing or feeding of peanut vines and hay.

c. Additional residue data for peanuts and hulls, including PHI's of 14 days and longer than 28 days, are needed so that RCB can determine whether residues increase with time and, if so, when a plateau is reached.

d. Pending RCB review of additional residue data which RCB now requests, a revised Section B/label may have to be submitted which proposes a PHI longer than 14 days (i.e. 28 days or longer).

e. Fractionation studies show that residues apparently do not concentrate in crude oil, refined oil, or dried peanut meal.

f. Residue data on the processed commodity soapstock should be provided.

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g. A revised Section B/label should be submitted which specifies a maximum of seven applications.

Meat, Milk, Poultry, and Eggs

Residues in meat, milk, poultry, and eggs were discussed in PP#5G3258 (L. Cheng, September 10, 1985). Excerpts from that review are repeated below:

"A conventional cattle feeding study was submitted in PP#0G1001. Three lactating dairy cattle were fed TBZ in the diet equivalent to 10 ppm continuously for 4 weeks. This was immediately followed by feeding the same cattle at 30 ppm TBZ dietary level for 4 additional weeks. Only milk samples were analyzed. No analyses on tissue samples were reported. At the 10 ppm feeding level no detectable residues of TBZ (<0.03 ppm) or 5-hydroxy-TBZ (<0.05 ppm) were noted in milk samples. From the 30 ppm feeding level, four samples contained 0.05 ppm and one had 0.17 ppm 5-hydroxy-TBZ. The remaining seven samples had no detectable 5-hydroxy-TBZ residues. All samples showed no detectable (<0.03 ppm) residues of TBZ."

"Some drug residue data published in J. Pharm. & Exp. Ther. 149, 263 (1965) were previously discussed in PP#1F1031 by E. Gunderson (memo of May 24, 1972). Calves and goats were orally dosed once at levels of 50, 110, 150 or 200 mg TBZ per kg body weight. Three days after the lowest dose (50 mg/kg approximates 1700 ppm in calves diet and 1250 ppm in goats diet), residues found in a calf were < 0.2 ppm in fat, heart, kidney, liver and muscle. Calf skin contained the highest residue of 0.46 ppm. When another calf was sacrificed 30 days after the same dose of 50 mg per kg, < 0.08 ppm TBZ residues were detected in all tissues. Five goats were dosed at the 50 mg/kg level. One goat sacrificed on day 1 showed residues of < 0.08 ppm in fat, 0.3 ppm in heart, 2.7 ppm in kidney, 1.1 ppm in liver and 0.3 ppm in skin. The day-17 goat showed < 0.08 ppm in fat, kidney or skin, and 0.2 ppm in heart and liver. The remaining goats contained < 0.08 ppm TBZ residues in all tissues on day 30. While the above data show low residues in tissues as a result of high feeding dose levels, these tissue residue studies were designed to support veterinary drug use and in this case, the TBZ label specifies a 30-day withdrawal period. Such withdrawal periods are not practical in pesticide uses since animals may be fed treated feed items up to time of slaughter (p. 3, memo dated May 24, 1972, PP#1F1031). The above data are no longer adequate in estimating TBZ residues in animal tissues from animals ingesting feed items containing high levels of TBZ residue (such as 150 ppm in grape pomace). The established 0.1 ppm meat tolerance may not be sufficient to cover the residues in animal tissues from all pesticide uses involving TBZ. We are also unable to project a meaningful meat tolerance level

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in the absence of appropriate feeding study data. A cattle continuous feeding study which includes the expected level of intake (this 1X level should represent the worst case estimate of the potential livestock exposure) and two exaggerated levels of 3X and 10X will be needed."

"A poultry feeding study was submitted in an amendment to PP#6F1860. Three-day old broiler chicks were fed a diet containing 0, 2, 20, 200, or 2000 ppm TBZ for 46 days. Four hours after the diet was removed, three males and three females at each dose level were sacrificed. At the 20 ppm feeding level, combined residues (in ppm) of TBZ were 0.017 to 0.023 in muscle, 0.024 to 0.028 in skin/fat, 0.068 to 0.121 in kidney and 0.056 to 0.081 in liver. Those resulting from the 200 ppm feeding level were 0.035 to 0.067 ppm, 0.056 to 0.102 ppm, 0.328 to 0.847 ppm and 0.204 to 0.631 ppm, respectively. Laying hens were also fed TBZ-containing diet at the same five levels for 21 days. The next three eggs laid by each hen after termination of dose were collected for residue analysis. Combined residues of TBZ were 0.007 to 0.022 ppm (whites) and 0.023 to 0.05 ppm (yolk) at the 20 ppm level, and 0.07 to 0.66 ppm (whites) and 0.044 to 1.31 ppm (yolk) at the 200 ppm level."

Assuming peanut vines and hay are not fed to livestock, peanut feed items are meal, hulls, and soapstock for beef cattle, meal and soapstock for dairy cattle, and meal and soapstock for poultry.

For beef and dairy cattle, feed items with tolerances of 10 to 150 ppm such as grape pomace, dehydrated apple pomace, dehydrated citrus pulp, citrus molasses, and cull potatoes would contribute to the diet containing the maximum residues.

RCB will reserve its conclusion on the adequacy of the established tolerances on meat, milk, poultry, and eggs resulting from the proposed use on peanuts until receiving residue data on peanut soapstock.

Other Considerations

An International Residue Limits (IRL) Status sheet is attached. A Codex proposal for thiabendazole on peanuts at 0.1 mg/kg is compatible with the U.S. proposed tolerances on peanuts. There are no Canadian or Mexican tolerances for thiabendazole on peanuts. Therefore, no compatibility questions exist with respect to Codex.

Attachment 1: International Residue Limits Status Sheet

cc: RF, Circu, Reviewer-N. Dodd, EAB, EEB, PP#6F3355, FDA, PMSD/ISB-Eldredge

RDI:J.H. Onley:4/29/86:R.D. Schmitt:4/30/86
TS-769:RCB:CM#2:RM810:X1681:N. Dodd:Kendrick & Co.:5/5/86

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL thiabendazole

PETITION NO 6F3355

N. Dodd

M. Metzger 4/23/86

CCPR NO. 065

Codex Status

☐ No Codex Proposal
Step 6 or above

Proposed U. S. Tolerances

Residue (if Step 9): thiabendazole [thiabendazole and 5-hydroxythiabendazole for animal products]

Crop(s)	Limit (mg/kg)
A01.1701 Peanuts	0.1 (on a shell-free basis)

Residue: thiabendazole [2-(4-thiazolyl)-benzimidazole]

Crop(s)	Tol. (ppm)
peanuts	0.1
peanut hulls	2.0

CANADIAN LIMIT

Residue: _____

Crop	Limit (ppm)
none (for peanuts or peanut hulls)	

MEXICAN TOLERANCIA

Residue: _____

Crop	Tolerancia (ppm)
none (for peanuts or peanut hulls.)	

Notes:

13071
3-5-86

REGISTRATION DIVISION DATA REVIEW RECORD

Confidential Business Information — Does Not Contain National Security Information (E.O. 12065)

1. CHEMICAL NAME [illegible]

2. IDENTIFYING NUMBER	3. ACTION CODE	4. ACCESSION NUMBER	TO BE COMPLETED BY PM
6F3335	230	261110	5. RECORD NUMBER 166732
			6. REFERENCE NUMBER 1
	981		7. DATE RECEIVED (EPA) 02-03-86
			8. STATUTORY DUE DATE NA
			9. PRODUCT MANAGER (PM) [illegible]
			10. PM TEAM NUMBER 21

14. CHECK IF APPLICABLE

- ☐ Public Health/Quarantine
- ☐ Minor Use
- ☐ Substitute Chemical
- ☐ Part of IPM
- ☐ Seasonal Concern
- ☐ Review Requires Less Than 4 Hours

TO BE COMPLETED BY PCB

11. DATE SENT TO HED/TSS 02/05/86
12. PRIORITY NUMBER 49
13. PROJECTED RETURN DATE 4/11/86

15. INSTRUCTIONS TO REVIEWER

A. HED ☐ Total Assessment - 3(c)(5)
☐ Incremental Risk Assessment - 3(c)(7) and/or E.L. Johnson memo of May 12, 1977.

B. SPRD (Send Copy of Form to SPRD PM)
☐ Chemical Undergoing Active RPAR Review
☐ Chemical Undergoing Active Registration Standards Review

C. ☐ BFSD
D. ☐ TSS/RD
E. ☒ Other

F. INSTRUCTIONS
[illegible handwritten instructions]

16. RELATED ACTIONS

17. 3(c)(1)(D)
☐ Use Any or All Available Information ☐ Use Only Attached Data
☐ Use Only the Attached Data for Formulation and Any or All Available Information on the Technical or Manufacturing Chemical.

18. REVIEWS SENT TO
☒ TB ☐ EEB ☐ EF ☐ PL
☒ RCB ☐ EFB ☐ CH ☐ BFSD

19.	To	TYPE OF REVIEW	Registration	Petition	EUP	SLN	Sec. 18	Inert	MNR. USE	Other
HED		TOXICOLOGY								
HED		ECOLOGICAL EFFECTS								
HED	✓	RESIDUE CHEMISTRY		1						
HED		ENVIRONMENTAL DATE								
RD/TSS		CHEMISTRY								
RD/TSS		EFFICACY								
RD/TSS		PRECAUTIONARY LABELING								
BFSD		ECONOMIC ANALYSIS								

20. ☒ Label Submitted with Application Attached
21. ☐ Confidential Statement of Formula
22. ☐ Representative Labels Showing Accepted Uses Attached
23. Date Returned to RD (to be completed by HED)
24. Include an Original and 4 (four) Copies of This Completed Form for Each Branch Checked for Review.

EPA Form 8570-13 (Rev. 11-81) PREVIOUS EDITIONS ARE OBSOLETE.

End Of Document

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

RCB

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

JUL 21 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: PP#6F3355. Mertect 340-F
EPA Reg. No. 618-75; Tox. Chem. No. 849A

TO: Mr. Henry M. Jacoby, PM No. 21
Fungicide - Herbicide Branch

FROM: Carlos A. Rodriguez CAR 7/3/86.
Review - Section No. VI
Toxicology Branch/HED (TS-769)

THRU: Jane E. Harris, Ph.D. 7/3/86 for JEH
Section Head, Review - Section VI
Toxicology Branch/HED (TS-769)

Petitioner: Merck & Co., Inc.
P.O. Box 2000 - WB D 360
Rahway, N.Y. 07065

Action Requested:

Merck & Co., Inc. requests that tolerances be established for use of its thiabendazole containing product Mertect 340 - F(42.3% Thiabendazole) to reduce the severity of early and late leafspots caused by Cercospora arachidicola and Cereosporidium pernonatum in/on peanuts 0.1 ppm and peanuts hulls at 2.0 ppm.

Recommendation(s):

The requested tolerances can be toxicology supported. RCB consideration permitting, Tox. Branch have no objectives to the issuance of this requested petition.

A. Inerts cleared under 180.100(c).

B. No new toxicity data submitted with this application.

Toxicity Data Considered in Setting This Action:

Study	Results	Category of Toxicity	Core - Classification
. Acute oral LD_{50} (male rat) (98.5% tech.)	LD_{50} = 3.97 g/kg (95% Conf. 2.92 - 2.40 g/kg)	III	Minimum
. (female rat) (95% Conf. = 2.14 - 5.85 g/kg)	LD_{50} = 3.54 g/kg	III	Minimum
. Acute oral LD_{50} (mouse) (42.28% formulation)	LD_{50} = 3.8 g/kg	III	Minimum

Study	Results	Category of Toxicity	Core - Classification
. Acute dermal LD_{50} (rabbit) 98.5% tech.)	LD_{50} > 4g/kg	III	Minimum
. Acute dermal LD_{50} (rabbit) (42.28% formulation)	LD_{50} > 5 ml/kg	III	Minimum
. Acute inhalation LC_{50} (98.5% tech.)	LC_{50} > 2.03 mg/L	III	Guideline
. Acute inhalation LC_{50} (42.28% formulation)	LC_{50} > 20 mg/L	IV	Minimum
. Primary eye irritation (rabbit) (98.5% tech.)	Slight irritation; cleared at 72 hrs.	III	Minimum
. Primary eye irritation (rabbit) (42.28% formulation)	Slight to moderate irritation; slight chemosis. Effects cleared by 72 hrs.	III	Minimum
. Primary dermal irritation (98.5% Tech.)	Slight erythema; cleared 48 hrs.	IV	Minimum
. Primary dermal irritation (42.28% formulation)	Slight erythema; cleared at 11th day	III	Minimum
* . 2-year rat feeding:	Systemic NOEL = 10 mg/kg/day Systemic LEL = 40 mg/kg (growth depression). Oncogenic potential negative at 160 mg/kg/day (highest dose tested) Dose levels tested: 10,40 and 160 mg/kg/day.		

Study	Results	Classification
. 2-Year dog feeding:	Systemic NOEL = 50 mg/kg/day; Systemic LEL = 125 mg/kg/day (decreased body weight). Dose levels tested: 20, 50, and 125 mg/kg/day.	
Lifetime oncogenic (mouse feeding)	Oncogenic NOEL > 5,330 ppm or 800 mg/kg/day (highest level tested). Systemic NOEL = 600 ppm or 100 mg/kg/day; Systemic LEL = 2000 ppm or 300 mg/kg/day (lower weight gain). Dose levels tested mg/kg/day), 2000 ppm (300 (mg/kg/day), 5,330 ppm (800 (mg/kg/day).	Minimum
* Rat teratology:	Teratogenic NOEL > 80 mg/kg/day (given by gavage, single dose tested) Maternal NOEL - < 80 mg/kg (only dose tested - lower mean inplantation sites)	
* Rabbit teratology:	Teratogenic NOEL > 800 mg/kg/day (highest dose tested). Maternal NOEL: 100 mg/kg/day; LOEL: 200 mg/kg/day (weight loss). Dose levels tested: 100, 200, 400 and 800 mg/kg/day.	
* 3-Generation reproduction (rat)	Reproduction NOEL = 20 mg/kg, reproductive LOEL = 40 mg/kg - decreased viability index of Fla. Dose levels tested: 20,40, and 80 mg/kg.	

. Mutagenicity Studies:

1.	Microbial (S. typhimurium) negative for induced revertants.	Acceptable
2.	Microbial (E. coli) negative for induced revertants.	Acceptable
3.	Host-mediated - negative	Acceptable

4. In vivo Bone marrow - negative for chromonsomal damage. Acceptable

5. Primary Bacterial DNA damage/repair - negative. Acceptable

6. In vitro cytogenetics - negative - no increase in chromosome breakage in human embryonic fibroblast cultures Acceptable

*

. Metabolism, absorption, distribution and excretion in man, dog, rat, sheep, goat, cattle and swine.

Rapidly metabolized in man. Radioactive agent in animal species in many respects were similar to those found in man. Tissues from laboratory animals were virtually free of radioactivity.

*

Studies not classified under the Grade Core Classification concept.

D. NO RPAR criteria have been exceeded and no regulatory actions are pending against registration.

E. The following studies 2-year rat feeding, 2-year dog feeding, lifetime mouse oncogenic, rabbit teratology and 3-generation rat reproduction have been used in support of this action. Since these studies were reviewed prior to the Grade Core Classification was instituted a thorough review of these studies will be done to determine if presently they satisfy a requirement. They will be reevaluated and Grade Core classified for the Registration Standard.

F. The mouse acute oral LD_{50} available in this formulation showed a similar toxicity to the rat acute oral LD_{50} in the technical product, therefore Tox. Branch believes that an additional acute oral LF_{50} in the rat is not necessary.

G. Data Gaps:

1) Sensitization study

2) Teratology study (2nd species)

Evaluation of the ADI

The acceptable daily intake (ADI) based on the 2 - year rat feeding study (NOEL 10, mg/kg/day) and using a hundred - fold safety factor, is calculated to be 0.1 mg/kg/day. The maximum permitted intake (MPI) for a 60 kg human is 6 mg/day.

The theoretical maximum residue contribution (TMRC) from existing tolerances published and Tox. approved for 1.5 kg diet is calculated to be 0.046515 mg/kg/day. The current action will increase the TMRC to 0.046524 mg/kg/day and utilize an additional 0.009 percent of the ADI occupying 46.5% of the ADI. The residues from peanuts will be insignificant in contributing to the dietary intake of thiabendazole. Computer printout is attached.

TOXICOLOGY BRANCH ADI PRINTOUT Date: 06/05/86

THE FOLLOWING INFORMATION WAS SUPPLIED BY THE USER:

Chemical name: THIABENDAZOLE
Caswell #849A
CFR No. 242

ADI = 0.1 MG/KG
Safety factor = 100

RESIDUE CONTRIBUTION OF PUBLISHED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
2	Apples	10.000		2.53	0.379500000
6	Avocados	10.000		0.03	0.004500000
7	Bananas	0.400		1.42	0.008520000
10	Beans, dry edible	0.100	4F2975	0.31	0.000465000
24	Carrots	10.000		0.48	0.072000000
26	Cattle	0.100		7.18	0.010770000
33	Citrus fruits	10.000		3.81	0.571500000
54	Eggs	0.100		2.77	0.004155000
62	Goats	0.100		0.03	0.000045000
69	Hogs	0.100		3.43	0.005145000
88	Mangoes	10.000		0.03	0.004500000
93	Milk and dairy products	0.100		28.62	0.042930000
97	Mushrooms	10.000	3F2883	0.03	0.004500000
109	Papayas	5.000		0.03	0.002250000
116	Pears	10.000		0.26	0.039000000
127	Potatoes	10.000	3F2882	5.43	0.814500000
128	Poultry	0.100		2.94	0.004410000
137	Rice	3.000		0.55	0.024750000
145	Sheep	0.100		0.19	0.000285000
148	Soybeans (oil)	0.100		0.92	0.001380000
154	Sugar, cane and beet	0.250		3.64	0.013650000
157	Sweet potatoes	0.020		0.40	0.000120000
170	Wheat	1.000	2F2603	10.36	0.155400000
191	Squash	1.000		0.11	0.001650000
208	Horses	0.100		0.03	0.000045000

TMRC	%ADI
0.036099 mg/kg/day (60kg BW, 1.5kg diet)	36.099500

RESIDUE CONTRIBUTION OF TOX-APPROVED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
23	Cantaloupe	12.000	2E2736	0.52	0.093600000
67	Grapes, not including raisins	10.000	1E2542	0.45	0.067500000

RESIDUE CONTRIBUTION OF TOX-APPROVED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
68	Corn, grain (field corn)	20.000	5G3258	1.00	0.300000000
93	Milk and dairy products	0.300	1E2542	28.62	0.128790000
152	Strawberries	5.000	2E2736	0.18	0.013500000
163	Tomatoes	0.500	2E2736	2.87	0.021525000

TMRC	%ADI
0.046515 mg/kg/day (60kg BW, 1.5kg diet)	46.514750

RESIDUE CONTRIBUTION OF NEW (PENDING) TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
115	Peanuts	0.100	6F3355	0.36	0.000540000

TMRC	%ADI
0.046524 mg/kg/day (60kg BW, 1.5kg diet)	46.523750

End Of Document

To: Nancy Dodd Date: 3/26/86

Petition No.: 6F3355 is assigned to you for review.

(1) To help us decide as soon as possible on a method tryout, please indicate before 4/2/86 (date), if there are any major deficiencies in the data of this petition and whether or not a tryout is needed.

(2) To meet permanent petition or substantive amendment deadlines, complete and submit your review to your Section Head ~~within 45 days~~, ~~in this case by~~ when completed (date).

(3) To meet temporary petition deadlines, complete and submit your review to your Section Head within 30 days, i.e., by i.e. (date). He will submit it for final approval to meet the 45 day Branch deadline for temporary tolerances.

Initial, date, and show this form to your Section Head.

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MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
P.O. BOX 2000, RAHWAY, NEW JERSEY 07065-0914

R. R. BUCK
ASSISTANT DIRECTOR
REGULATORY AFFAIRS

(201) 750-8657

January 30, 1986

9F3335

Mr. Henry M. Jacoby
Fungicide-Herbicide Branch
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Crystal Mall #2, Room 229
Arlington, VA 22210

Dear Mr. Jacoby:

We are writing with respect to our product MERTECT 340-F, EPA Reg. No. 618-75.

We propose to revise the label to include a new use for the product to reduce the severity of early and late leafspots caused by Cercospora arachidicola and Cereosporidium pernonatum on growing peanuts.

Five copies of a proposed supplemental label, including the new use and residue data to support the establishment of a tolerance, are attached, as well as a check for $2,000 to cover the cost of the review.

Very truly yours,

Robert R. Buck

RRB/gh

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MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
P.O. BOX 2000, RAHWAY, NEW JERSEY 07065-0914

R. R. BUCK
ASSISTANT DIRECTOR
REGULATORY AFFAIRS

(201) 750-8657

January 30, 1986

Registration Division
Environmental Protection Agency
Washington, D. C. 20460

Dear Sirs:

The undersigned, Merck & Co., Inc., submits this petition pursuant to section 408(d)(1) of the Federal Food, Drug and Cosmetic Act with respect to the pesticide chemical MERTECT 340-F Fungicide.

Attached hereto, in duplicate and constituting a part of this petition, are the following:

A. The name, chemical identity and composition of the pesticide chemical.

B. The amount, frequency and time of application of the pesticide chemical.

C. Full reports of investigations made with respect to the safety of the pesticide chemical.

D. The results of tests on the amount of residue remaining, including a description of the analytical method used.

E. Practicable methods for removing residue that exceeds any proposed tolerance.

F. Proposed tolerances for the pesticide chemical if tolerances are proposed.

G. Reasonable grounds in support of the petition.

Enclosed is a check for $2,000, payable to the Environmental Protection Agency to cover clerical operations, initial administrative review and the cost incurred in considering the petition after it has been filed.

Very truly yours,

Robert R. Buck

RRB/gh
Enclosures

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End Of Document

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Form Approved. OMB No. 2000-0483. Approval expires 9-30-87

EPA

ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAM (TS-767)
WASHINGTON, D.C. 20460

APPLICATION FOR PESTICIDE: ☐ REGISTRATION ☒ AMENDMENT A

Please read instructions on reverse before completing.

SECTION I

1. COMPANY/PRODUCT NO.	2. DATE	3. PRODUCT MANAGER	4. PROPOSED CLASSIFICATION
618-75	January 30, 1986	Mr. Henry M. Jacoby	☒ GENERAL ☐ RESTRICTED

5. NAME AND ADDRESS OF APPLICANT (Include ZIP Code)

MERCK & CO., INC.
P.O. Box 2000 - WB D-360
Rahway, NJ 07065
Attention: R. R. Buck
Assistant Director

☐ CHECK IF THIS IS A NEW ADDRESS

6. PRODUCT NAME

MERTECT 340-F

SECTION II

1. SUBJECT OF AMENDMENT

☐ RESUBMISSION IN RESPONSE TO AGENCY LETTER DATED _____

☐ FINAL PRINTED LABEL IN RESPONSE TO AGENCY LETTER DATED _____

☒ OTHER (explain below)

A new claim to reduce the severity of early and late leafspots caused by Cercospora arachidicola and Cereosporidium pernonatum on growing peanuts has been added to the label. Copies of the proposed supplemental label are attached as well as residue data to support a tolerance for use on peanuts.

SECTION III

1. WILL THIS PRODUCT BE PACKAGED IN:

CHILD-RESISTANT PACKAGING ☐ YES ☐ NO

UNIT PACKAGING ☐ YES ☐ NO

If YES; unit pkg. wt. _____ No. per container _____

WATER-SOLUBLE PACKAGING ☐ YES ☐ NO

If YES, pkg. wt. _____ No. per container _____

2. TYPE OF CONTAINER

☐ METAL ☐ PLASTIC ☐ GLASS ☐ PAPER ☐ OTHER (Specify)

3. LOCATION OF NET CONTENTS ☐ LABEL ☐ CONTAINER

4. SIZE(S) OF RETAIL CONTAINER

5. LOCATION OF LABEL DIRECTIONS ☐ ON LABEL ☐ ON MATERIAL ACCOMPANYING PRODUCT

6. MANNER IN WHICH LABEL IS AFFIXED TO PRODUCT ☐ LITHOGRAPH ☐ OTHER (Specify) ☐ PAPER GLUED ☐ STENCILED

SECTION IV

1. CONTACT POINT (Complete items directly below for identification of individual to be contacted, if necessary, to process this application).

NAME: ROBERT R. BUCK

TITLE: Assistant Director

TELEPHONE NO. (Include Area Code): 201-750-8657

2. SIGNATURE: Robert R Buck

3. TITLE: Assistant Director

4. TYPED NAME: ROBERT R BUCK

5. DATE SIGNED: 1/30/86

6. DATE APPLICATION RECEIVED (Stamped)

EPA Form 8570-1 (Rev. 5-81) PREVIOUS EDITION IS OBSOLETE.

13544

R105033

Chemical:	**Thiabendazole**
PC Code:	**060101**
HED File Code	**11500 Petition Files Chemistry**
Memo Date:	**02/02/2005**
File ID:	**00000000**
Accession Number:	***412-05-0092***

HED Records Reference Center
02/14/2005