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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Date: 1/12/99

SUBJECT: **Thiabendazole Reregistration**. 860.1500 and 860.1340-Response to Agency Reviews for Magnitude of the Residue in Mushrooms, Sweet Potatoes, Potatoes, and Potato Processed Commodities; New Field Trials for Sweet Potatoes Grown from Treated Seed Roots; and Storage Stability Data for Sweet Potato.

DP Barcode No.: D214188.
Reregistration Case No.: 2670.
PC Code: 060101.
MRID No.: 43531001, 43531002, and 43547601.

FROM: Sherrie L. Mason, Chemist
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THROUGH: Alan Nielsen, Branch Senior Scientist
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Attached is a review of studies submitted for the magnitude of the residue in mushrooms, sweet potatoes, potatoes, and potato processed commodities; new field trials for sweet potatoes grown from treated seed roots; and storage stability data for sweet potato. The submission was reviewed by Dynamac Corporation under the supervision of HED. This information has undergone secondary review in reregistration branch 2 and is consistent with current Agency policies.

1. Mushrooms (MRID #: 43531001):

The submitted storage stability data for thiabendazole (TBZ) and benzimidazole (BNZ) in frozen mushrooms are adequate and indicate that these compounds are stable in/on frozen mushrooms for up to 28 months. These data support the available mushroom field trials.

The available field trial data for TBZ residues in/on mushrooms are adequate and support the established 40 ppm tolerance for TBZ residues in/on mushrooms.

2. **Sweet Potato, Potato, and Processed Fractions (MRID #: 43531002):**
The available residue studies reflecting the post-harvest treatment of white potatoes are adequate and support the established 10 ppm tolerance for TBZ residues in/on white potatoes.

The Agency concludes that residues of BNZ (free and conjugated) are unlikely to contribute significantly to the total TBZ residues in/on white potatoes and potato processed fractions given the highest potential TBZ residues in/on white potatoes result from post-harvest applications.

As the maximum combined residues of TBZ and BNZ may exceed the established 0.02 ppm tolerance, the tolerance for residues in/on sweet potatoes should be increased to 0.05 ppm.

The available potato processing study is adequate. Residues of TBZ did not concentrate in white potato flakes, chips, or wet peel, but concentrated by 16.6x in dry peel.

3. **Sweet Potatoes grown from Seed Roots (MRID #: 43547601, vol. 1-5):**
Merck's HPLC/fluorescence detection method M-046 is adequate for determining residues of TBZ *per se* in/on potatoes (sweet and white).

Merck's HPLC/fluorescence detection method M-048 is adequate for determining residues of BNZ (free and conjugated) in/on potatoes (sweet and white) and potato processed commodities.

The available storage stability data indicate that TBZ and BNZ are stable in frozen potatoes and wet potato peel for up to 27 months. Although no decline in residues of TBZ and BNZ were observed in potatoes stored frozen up to 27 months, the registrant's extrapolation of these data to estimate storage stability at 52 months is inappropriate as the extrapolation is based upon only three time points and the last analysis (27 months) represents only half of the entire 52 month storage interval.

Storage stability data are required to support the sweet potato field studies. Definitive analyses of sweet potato samples using improved methodology were conducted after 51-52 months of storage at ≤-20°C. If stored fortified samples of potatoes are still available, analysis of these samples could resolve this deficiency.

As TBZ is applied to sweet potatoes as a pre-planting application and data from the metabolism study on sugar beets (MRID #: 41872901-41872903; Thiabendazole Phase V Review by L. Cheng to F. Rubis on 3/11/92) and the confined rotational crop study indicate that BNZ (free and conjugated) is present in root crops, confined rotational crop data are required for residues of both TBZ and BNZ (free and conjugated) in/on sweet potatoes.

The available sweet potato residue data on mature sweet potatoes grown from seed roots treated with

TBZ as a 2 minute dip at 0.24 lb ai/7.5 gal. are adequate pending submission of acceptable storage stability data.

EXECUTIVE SUMMARY

Deficiencies in the Mushrooms (MRID #: 43531001): There are no deficiencies; therefore these data are acceptable.

Deficiencies in the Sweet Potato, Potato, and Processed Fractions (MRID #: 43531002): There are no deficiencies that would seriously compromise the interpretation of these data; however, **The tolerance of TBZ residues in/on sweet potatoes will be reassessed at the time of the Thiabendazole RED.**

Deficiencies in the Sweet Potatoes grown from Seed Roots (MRID #: 43547601 vol. 1-5): There are deficiencies that would seriously compromise the interpretation of these data. The registrant's extrapolation of these data to estimate storage stability at 52 months is inappropriate as the extrapolation is based upon only three time points and the last analysis (27 months) represents only half of the entire 52 month storage interval. **Storage stability data are required to support the sweet potato field studies. Definitive analyses of sweet potato samples using improved methodology were conducted after 51-52 months of storage at ≤-20°C. If stored fortified samples of potatoes are still available, analysis of these samples could resolve this deficiency. Potato dry peel is no longer listed (Table 1, OPPTS Guideline 860.1000) as a regulated processed commodity of potatoes; therefore, separate tolerances for potato processed commodities are not required, and the current tolerance for residues of TBZ in potato processing waste should be revoked.** Data from the metabolism study on sugar beets and the confined rotational crop study indicate that BNZ (free and conjugated) is present in root crops. As TBZ is applied to sweet potatoes as a pre-planting application, **data are required for residues of both TBZ and BNZ (free and conjugated) in/on sweet potatoes.**

cc: Sherrie L. Mason (RRB2), Thiabendazole List B File, Thiabendazole Subject File, RF, LAN.
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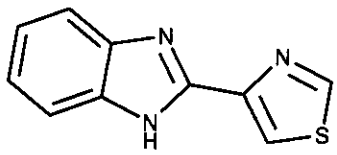
7509C: RRB2: S. Mason: CM#2:Rm 718Q: 703-305-0563: 1/12/99.

Thiabendazole



(PC Code 060101. Case No. 2670)

CBRS No. 15434; DP Barcode D214188

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

The Thiabendazole Phase 4 Review (C. Olinger, 2/20/91) required data depicting thiabendazole residues in/on mushrooms, sweet potatoes, potatoes, and potato processed commodities treated with thiabendazole at the maximum label rates specified for the respective crops. In response, Merck & Company, Inc. submitted residue data for thiabendazole (TBZ) and benzimidazole (BNZ) in/on mushrooms (1992, MRID 42598901) reflecting direct applications. Review of these data by HED (DP Barcode D186572, 11/22/93, D. Miller) noted the need for additional data on the storage stability of residues in mushrooms. The review also noted the possibility of over tolerance residues resulting from the use of TBZ at the maximum label rate. Merck also submitted residue data for TBZ residues in/on sweet potatoes (1993, MRID 42660301) treated as seed pieces prior to planting and in/on potatoes and potatoes processed commodities (1993, MRID 42660302) treated post-harvest. After reviewing these submissions, HED (DP Barcode D189323, 8/3/93, J. Abbotts) required residue data for BNZ in/on sweet potatoes, additional storage stability data for TBZ and BNZ in potatoes, development of tolerance enforcement methodology for determining BNZ (free and conjugate), and modification of label directions of the use on potatoes.

In its current submissions (1995, MRIDs 43547601, 43531001 and 43531002), Merck has responded to the deficiencies cited in the above mushroom, sweet potato, potato, and potato processing studies. These submissions are reviewed in this memoranda for adequacy in fulfilling outstanding residue chemistry data requirements. The Conclusions and Recommendations stated in this document pertain only to analytical methodology, the storage stability of residues, and magnitude of the residue in/on mushrooms, sweet potatoes, potatoes, and potato processed commodities.

The nature of the residue in plants and animals is adequately understood based on plant

metabolism studies on soybean, sugar beet, and wheat, and animal metabolism studies on poultry, and goats. HED Metabolism Committee has concluded that residues of concern in plants are TBZ and BNZ and its conjugates (L. Cheng; CBRS No. 8192, 3/11/92). The residues of concern in animals are TBZ, 5-OH-TBZ (free and conjugated), and BNZ (L. Cheng; CBRS Nos. 8719 and 8930, 3/2/92).

Tolerances for residues of thiabendazole (2-(4-thiazolyl)benzimidazole) in or on raw agricultural commodities and processed foods and feeds are currently expressed in terms of TBZ per se [40 CFR §180.242(a), §185.5550, and §186.5550(a)]. Tolerance for residues of TBZ in animal commodities are currently expressed as the combined residues of TBZ and its metabolite 5-OH-TBZ [40 CFR §180.242(b)]. Methods are available for determining residues of TBZ per se in or on plant commodities and are listed in PAM, Vol. II, as Methods I, A, B, and C. A method is also available for determining residues of TBZ and 5-OH-TBZ in milk, and is listed in PAM, Vol. II, as Method D.

Codex Maximum Residue Limits (MRLs) for TBZ are presently expressed in terms of TBZ *per se* for plant commodities and in terms of the combined residues of TBZ and 5-OH-TBZ for animal commodities. Issues regarding the compatibility of the U.S. tolerances and Codex MRLs will be addressed when the reregistration eligibility decision for thiabendazole is made.

CONCLUSIONS AND RECOMMENDATIONS

1a. Merck's HPLC/fluorescence detection method M-046 is adequate for determining residues of TBZ *per se* in/on potatoes (sweet and white). The validated limit of quantitations (LOQs) for TBZ are 0.05 ppm in/on white potatoes and 0.005 ppm in/on sweet potatoes.

1b. Merck's HPLC/fluorescence detection method M-048 is adequate for determining residues of BNZ (free and conjugated) in/on potatoes (sweet and white) and potato processed commodities. The validated LOQ for BNZ residues is 0.01 ppm in/on sweet potatoes, 0.02 ppm in/on white potatoes, and 0.2 ppm in/on dry potato peel.

2a. The submitted storage stability data for TBZ and BNZ in frozen mushrooms are adequate and indicate that these compound are stable in frozen mushrooms for up to 28 months. These data support the available mushroom field trials, in which samples were stored at -23°C for 15 to 18 months prior to analysis.

2b. The available storage stability data indicate that TBZ and BNZ are stable in frozen potatoes and wet potato peel for up to 27 months. Although no decline in residues of TBZ and BNZ were observed in potatoes stored frozen up to 27 months, the registrant's extrapolation of these data to estimate storage stability at 52 months is inappropriate as the extrapolation is based upon only three time points and the last analysis (27 months) represents only half of the entire 52 month storage interval.

2c. Storage stability data are required to support the sweet potato field studies. Definitive analyses of sweet potato samples using improved methodology were conducted after 51-52 months of storage at ≤-20°C. If stored fortified samples of potatoes are still available, analysis of these samples could resolve this deficiency.

3. The available field trial data for TBZ residues in/on mushrooms are adequate and support the established 40 ppm tolerance for TBZ residues in/on mushrooms.

4a. The available residue studies reflecting the post-harvest treatment of potatoes are adequate and support the established 10 ppm tolerance for TBZ residues in/on potatoes. Residue of TBZ *per se* were 1.2-7.3 ppm in/on potatoes following the last of two post-harvest mist applications of TBZ at 0.0125 lb ai/ton (1x).

4b. Given that post-harvest applications result in the highest potential TBZ residues in/on potatoes, HED concludes that residues of BNZ (free and conjugated) are unlikely to contribute significantly to the total TBZ residues in/on potatoes and potato processed fractions.

5a. As TBZ is applied to sweet potatoes as a pre-planting application and data from the metabolism study on sugar beets and the confined rotational crop study indicate that BNZ (free and conjugated) is present in root crops, data are required for residues of both TBZ and BNZ (free and conjugated) in/on sweet potatoes.

5b. The available sweet potato residue data are adequate pending submission of acceptable storage stability data (See conclusion 2c). Residues of TBZ were <0.005-0.015 ppm in/on mature sweet potatoes grown from seed roots treated with TBZ as a 2 minute dip at 0.24 lb ai/7.5 gal. Residues of BNZ (free and conjugated) were non-detectable (<0.007 ppm), and the combined residues of TBZ and BNZ were <0.012-<0.022 ppm.

5c. As the maximum combined residues of TBZ and BNZ may exceed the established 0.02 ppm tolerance, the tolerance for residues in/on sweet potatoes should be increased to 0.05 ppm. The tolerance of TBZ residues in/on sweet potatoes will be reassessed at the time of the Thiabendazole RED.

6. The available potato processing study is adequate. Residues of TBZ did not concentrate in potato flakes, chips, and wet peel, but concentrated by 16.6x in dry

peel. However, potato dry peel is no longer listed (Table 1, OPPTS Guideline 860.1000) as a regulated processed commodity of potatoes. Therefore, separate tolerances for potato processed commodities are not required, and the current tolerance for residues of TBZ in potato processing waste should be revoked.

DETAILED CONSIDERATIONS

Residue Analytical Methods

In conjunction with the registrant's responses to HED reviews of potato residue studies, Merck submitted descriptions (1995, MRID 43547601) for two new HPLC/Fluorescence detection methods for determining TBZ residues in/on white and sweet potatoes and potato processed commodities along with method validation data. These methods are similar to the current enforcement methods in that residues are extracted with ethyl acetate (EtOAc) and are quantified fluorometrically. However, the new methods employ additional clean-up procedures and utilize HPLC/fluorescence detection for separating and quantifying residues.

Merck Method M-046 is for determining TBZ *per se* in/on whole potatoes (white and sweet). Residues are extracted from homogenized samples with EtOAc. The EtOAc-soluble residues are then loaded onto a propyl sulfonic acid (PRS) solid phase extraction (SPE) column preconditioned by washing successively with 1% H_3PO_4 in methanol (MeOH)/water (80/20, v/v), MeOH, and EtOAc. After sample loading, the SPE column is allowed to run dry for 15 minutes, and residues are then eluted from the column using 0.1 M KH_2PO_4 in acetonitrile (ACN)/water (30/70, v/v). Residues of TBZ are then analyzed by cation exchange (benzene sulfonic acid column) HPLC using an isocratic mobile phase of 0.05 M KH_2PO_4 in ACN/water (25/75, v/v) adjusted to pH 3.4. Residues are quantified using fluorescence detection (excitation - 305 nm, emission - 380 nm). The validated LOQs for TBZ are 0.05 ppm in/on white potatoes and 0.005 ppm in/on sweet potatoes; and the estimated limit of detections (LODs) for TBZ are 0.0025 ppm in/on sweet potatoes and 0.025 ppm in/on white potatoes.

For method validation, the registrant fortified triplicate control samples of white potatoes with TBZ at 0.05-20 ppm and triplicate control samples of sweet potatoes with TBZ at 0.005-0.1 ppm. Results of the method validation are presented in Table 1. Overall method recoveries of TBZ were 98-104% from white potatoes and 89-99% from sweet potatoes. Apparent residues of each analyte were <LOD in the two control samples analyzed for each crop. Adequate sample calculations, raw data, and representative chromatograms were provided. These data indicate that the HPLC/fluorescence method M-046 is adequate for determining residues of TBZ *per se* in/on potatoes (sweet and white).

Table 1. Recovery of TBZ from fortified control samples of white and sweet potatoes using Merck's HPLC/fluorescence detection Method M-046.

Matrix	Fortification level (ppm)	% Recovery
White potatoes	0.05	98.6, 97.9, 99.9
	1.0	99.5, 97.6, 98.9
	10.0	100.3, 99.0, 99.7
	20.0	103.7, 103.5, 103.6
Sweet potatoes	0.005	90.5, 89.4, 91.1
	0.02	97.9, 99.2, 98.4
	0.1	96.5, 93.1, 93.7

Merck Method M-048 is for determining total BNZ (free and conjugated) in/on potatoes (sweet and white) and processed potato commodities. Dry potato peel samples are hydrated with water for 1 hour prior to extraction. Residues are extracted from homogenized samples with 0.025 M HCl and filtered. The extract is adjusted to pH 5 and residues are incubated with β-glucosidase for 24 hours at 38 C. After cooling, the resulting hydrolysate is adjusted to pH 8, and residues are extracted into EtOAc. The EtOAc-soluble residues are then loaded onto a preconditioned PRS SPE column. After loading, the SPE column is allowed to run dry for 15 minutes, and residues are then eluted from the column using 0.1 M KH_2PO_4 in ACN/water (30/70, v/v). Residues of BNZ are then analyzed by cation exchange HPLC using an isocratic mobile phase of 0.05 M KH_2PO_4 in ACN/water (25/75, v/v) adjusted to pH 3.2. Residues of BNZ are quantified using fluorescence detection (excitation - 265 nm, emission - 380 nm). The validated LOQ for BNZ residues is 0.01 ppm in/on sweet potatoes, 0.02 ppm in/on white potatoes, and 0.2 ppm in/on dry potato peel. The estimated LOD is 0.007 ppm for whole potatoes (sweet and white) and 0.07 ppm for dry peel.

For method validation, the registrant fortified triplicate control samples of sweet potatoes with BNZ at 0.01, 0.02, and 0.1 ppm, and duplicate control samples of white potatoes and dry potato peels with BNZ at 0.02 and 0.2 ppm, respectively. Samples were also fortified with TBZ; however, recoveries of TBZ were not reported. Results of the method validation are presented in Table 2. Method recoveries of BNZ were 90-99% from sweet potatoes, 92-99% from whole potatoes, and 93-107% from dry potato peel. Apparent residues of each analyte were <LOD in control samples. Adequate sample calculations, raw data, and representative chromatograms were provided. These data indicate that the HPLC/fluorescence method M-048 is adequate for determining residues of BNZ in/on potato and processed potato commodities.

Table 2. Recovery of free and conjugate BNZ from fortified control samples of white and sweet potatoes and potato dry peel using Merck's HPLC/fluorescence detection Method M-048.

Matrix	Fortification level (ppm)	% Recovery
Sweet potatoes	0.01	90.1, 98.3, 98.8
	0.02	82.7, 84.3, 85.6
	0.1	90.8, 90.1, 87.1
White potatoes	0.02	92.0, 99.3
Potato dry peel	0.2	93.1, 107.4, 105.3

Storage Stability Data

In response to HED's review (D. Miller, 11/22/93) of mushroom field trail data, Merck submitted data (1995, MRID 43531001) on the stability of TBZ and BNZ in frozen mushrooms. Preliminary storage stability data (0-, 3-, and 6-month data) were reviewed originally with the field trial data. The current submission includes data from 12-month (TBZ only) and 28-month analyses of fortified stored samples.

Duplicate control samples of mushrooms were separately fortified with TBZ at 0.1 and 50 ppm and with BNZ at 0.02 and 0.1 ppm. Samples were analyzed after 0, 3, 6, 12 (TBZ only), and 28 months of storage at -23°C. At each storage interval, duplicate stored and freshly fortified samples from each fortification level were analyzed along with a single control sample. All samples were analyzed using Merck SAP 500-M-021, which was discussed in the previous review. Results of the analyses are presented in Table 3. Apparent residues of TBZ were $\leq$0.01 ppm in two control samples; apparent residues of BNZ in control samples were not reported.

The submitted storage stability data are adequate and indicate that TBZ and BNZ are stable in frozen mushrooms for up to 28 months. These data support the available mushroom field trials in which samples were stored at -23°C for 15 to 18 months prior to analysis.

Table 3. Stability of TBZ and BNZ in mushrooms, whole potatoes, and wet potato peel stored at -23 C.

Matrix/ analyte	Fortification level (ppm)	Storage Interval (months)	Freshly fortified Recoveries (%) [a]	Stored Sample Recoveries (%) [a]
Mushrooms				
TBZ	0.1	12	97, 99	94, 100
		28	97, 103	94, 99
	50	12	103, 97	98, 104
		28	97, 97	97, 103
BNZ	0.02	28	111, 111	96, 99
	0.1	28	106, 115	108, 89
Whole white potatoes				
TBZ	0.2	0	99, 93	104, 95
		3	103, 99	100, 102
		27	109, 97	128, 93
BNZ	0.05	0	105, 108	105, 103
		3	102, 103	98, 102
		27	102, 104	99, 102
Wet potato peels				
TBZ	0.5	0	106, 102	107, 108
		3	110, 104	107, 103
		27	98, 92	96, 92
BNZ	0.1	0	104, 104	113, 106
		3	99, 94	94, 94
		27	96, 97	93, 93

[a] Recovery values for potato matrices are the average of duplicate analyses from a single sample.

[b] Preliminary data (0-, 3-, and 6-month analyses) indicated that TBZ and BNZ were stable in mushrooms for up to 6 months.

In response to HED's review (J. Abbotts, 8/3/93) of potato field trail and processing data, Merck has submitted data (1995, MRID 43547601) on the stability of TBZ and BNZ in frozen potatoes and wet potato peel for up to 27 months. Preliminary data (0- and 3-month analyses) from the storage stability study were reviewed along with the field and processing residue data. The current submission includes data from the final 27-month storage interval.

Duplicate control samples of potatoes and wet potato peel were fortified with TBZ at 0.2 and 0.5 ppm, respectively, and with BNZ at 0.05 and 0.1 ppm, respectively. Samples were analyzed after 0, 3, and 27 months of storage at -23°C. At each storage interval, duplicate stored and freshly fortified samples were analyzed along with a single control sample. All samples were analyzed using Merck SAP 500-P-021, which was discussed in the previous review. Results of the analyses are presented in Table 3. Apparent residues of TBZ were ≤0.02 ppm in control

samples, and apparent residues of BNZ were non-detectable (level unspecified) in control samples. Adequate sample calculations, raw data, and representative chromatograms were provided.

The submitted storage stability data indicate that TBZ and BNZ are stable in frozen potatoes and wet potato peel for up to 27 months. The registrant also stated that extrapolation of the potato storage stability data indicates that TBZ and BNZ would be stable under frozen conditions for up to 52 months. Using recovery data from the 0-, 3-, and 27-month analyses, the registrant calculated potential recoveries at 52 months assuming first order kinetics and calculating a rate equation.

Although the available storage stability data showed no decline in TBZ and BNZ in potatoes stored frozen up to 27 months, the extrapolation of these data to estimate recoveries at 52 months is inappropriate because the extrapolation is based upon only three time points and because the last analysis (27 months) represents only half of the entire 52 month storage interval.

The available storage stability data on potato commodities supports the potato field trials and processing study as residues of TBZ were determined in frozen whole potatoes and processing fractions within 20 months of sampling and because HED has concluded that residues of BNZ are unlikely to contribute significantly to the total TBZ residues in potato commodities treated post-harvest.

However, the above storage stability data do not support the sweet potato field trails as samples from these trials were stored frozen for up to 52 months prior to definitive determinations of TBZ and BNZ (free and conjugated).

If stored fortified samples of whole potatoes are still available from the above storage stability study, analysis of TBZ and BNZ remaining in these samples could resolve the question of the stability of these residues in sweet potato samples from the field trails.

Magnitude of the Residue in Plants

Mushrooms

A tolerance of 40 ppm has been established for residues of TBZ *per se* in/on mushrooms [40 CFR §180.242(a)]. A REFS search dated 10/15/97 listed one TBZ end-use product, a 3.8 lb/gal FlC (EPA Reg. No. 100-889) registered to Novartis Crop Protection, Inc. for use on mushrooms. This product is registered for application to mushrooms by direct spray or in irrigation water at casing, fuzzing, pinning, and between breaks. The first application can be made at up to 0.24 lb ai/1000 ft^2, with three subsequent applications at a maximum of 0.12 lb ai/1000 ft^2 each, for a maximum of 0.6 lb ai/1000 ft^2/crop. A PHI of 12 hours is specified.

Field trial data reflecting the above registered use on mushrooms were submitted by Merck and reviewed by HED (D. Miller, 11/22/93). HED concluded that the available TBZ residue data on mushrooms would be adequate and would support the established 40 ppm tolerance provided that (i) the registrant submit data depicting the stability of TBZ and BNZ in mushrooms stored at -23°C for up to 18 months, and (ii) amend the labeled use pattern on mushrooms to limit direct spray applications to a maximum of 0.12 lb ai/1000 ft^2 per application.

In response, Merck has submitted storage stability data (1995; MRID 43531001) indicating that TBZ and BNZ are stable in frozen mushrooms for up to 28 months. These data are adequate and are discussed above in the Storage Stability Data section. The registrant has also submitted a copy of an amended label for the 3.8 lb/gal FlC formulation that limits direct spray applications to a maximum of 0.12 lb ai/1000 ft^2/application. With the submission of this information, all deficiencies relating to the mushroom field trial data have been resolved.

Potatoes

A tolerance of 10 ppm has been established for residues of TBZ *per se* in/on potatoes [40 CFR §180.242(a)]. A REFS search dated 10/15/97 identified two TBZ products, a 3.8 lb/gal FlC (EPA Reg. No. 100-889) and a 89% WDG (EPA Reg. No. 100-891), registered to Novartis Crop Protection, Inc. for use on potatoes. These products are registered for post-harvest applications to potatoes as a mist application at a rate of 0.0125 lb ai/2000 lb tubers, followed after an unspecified storage interval by a mist application at the same rate or a 20-second dip application at 0.0125 lb ai/gal water. An application may also be made to seed tubers prior to cutting.

In response to the TBZ Phase 4 Review, Merck submitted data (1993, MRID 42660302) on residues of TBZ and BNZ (free) in/on potatoes sampled following the last of two post-harvest applications of TBZ at 1x. In its review of these data, HED (J. Abbotts, 8/3/93) concluded that the available data on residues of TBZ *per se* in/on potatoes would be adequate provided additional storage stability data were provided and labels were amended to reflect a minimum 30-day retreatment interval. HED reserved judgement on the need for additional residue data on BNZ until validated methodology is available for determining free and conjugated BNZ in/on

potatoes.

In response to HED's review, Merck submitted (1995, MRIDs 43531002 and 43547601) descriptions of new HPLC/fluorescence methodology for determining TBZ and BNZ (free and conjugate) in potato commodities, supporting storage stability data for TBZ and BNZ residues in/on potatoes and dry potato peel, a sample label with amended use directions for potatoes, and residue data on free and conjugated BNZ in/on potatoes treated at 1x. In addition, the registrant requested that HED waive requirements for determining BNZ (free and conjugated) in/on potato commodities.

The HPLC/fluorescence methods, Merck Methods M-046 and M-048 (discussed in the above Residue Analytical Methods section), for determining TBZ and BNZ (free and conjugated) are adequate. The deficiency pertaining to methodology for residues in/on potatoes is resolved.

Samples from the potato residue studies were stored at -26°C for 19 to 20 months prior to analysis. The available storage stability, discussed above, indicate that residues of TBZ and BNZ are stable in frozen potato commodities for up to 27 months. This deficiency is resolved.

The registrant provided a sample label of the 3.8 lb/gal FlC formulation of TBZ which includes amended use directions for potatoes. The amended label now specifies a minimum 30-day re-treatment interval between the two post-harvest applications. This deficiency is resolved.

Along with the above data, the registrant presented arguments for waiving the requirement for data on residues of BNZ (free and conjugated) in/on potato commodities. These included two published reports pertaining to the breakdown of TBZ. In one article (Jacob *et al.*, J. Agric. Food Chem. 1975, Vol. 23, No. 4 pp. 704-708), [^{14}C]TBZ was shown to breakdown to BNZ on sugar beet leaves exposed to natural sunlight but not on leaves exposed to artificial light, indicating that the formation of BNZ results from photolysis of TBZ rather than by direct plant metabolism. In the second article (Tisdale and Lord, Pestic. Sci. 1973, Vol. 4, pp. 121-130), [^{14}C]TBZ was applied to potatoes that were then stored under simulated commercial storage conditions. No metabolism of TBZ was observed in potatoes storage for up to 3 months. Together these reports indicate that BNZ is unlikely to comprise a significant component of the residues in/on potatoes placed in storage following the post-harvest application of TBZ.

In addition to the above articles, the registrant presented supplemental data on residues of BNZ (free and conjugated) in/on potato. Selected treated samples of potatoes from the original residue study were analyzed for BNZ residues using Merck Method M-048. Samples had been held in frozen storage for up to 51 months prior to this analysis. A total of four (out of 16) treated samples and one control sample were analyzed. Residues of BNZ (free and conjugated) in each of these samples were <0.01 ppm. Previous analyses reported in the original study found that residues of TBZ *per se* were 1.2-7.3 ppm in/on potatoes treated post-harvest.

Based on the above information, HED concurs with the registrant that BNZ (free and conjugated)

is not likely to contribute significantly to total TBZ residues in/on potatoes treated post-harvest with TBZ. Additional data on BNZ residues in/on potatoes are not required.

The available residue studies reflecting the post-harvest treatment of potatoes are adequate and support the established 10 ppm tolerance for TBZ residues in/on potatoes.

Sweet Potatoes

A tolerance of 0.02 ppm has been established for residues of TBZ *per se* in/on sweet potatoes [40 CFR §180.242(a)]. A REFS search dated 10/15/97 listed two TBZ products, a 3.8 lb/gal FlC (EPA Reg. No. 100-889) and a 89% WDG (EPA Reg. No. 100-891), registered to Novartis Crop Protection, Inc. for use on sweet potatoes. These products are registered for a pre-planting dip application of TBZ to sweet potato seed roots at 0.24 lb ai/7.5 gal water for up to 2 minutes. Seed pieces must be planted immediately following treatment and the use of treated roots for food or feed is prohibited.

Field trial data from four test sites reflecting the above registered use on sweet potatoes were submitted by Merck and reviewed by HED (J. Abbotts, 8/3/93). HED concluded that the available TBZ residue data on sweet potatoes was inadequate because residues of BNZ (free and conjugated) were not determined and because data supporting the stability of TBZ in sweet potatoes over the 24-month storage interval were not provided. In addition, residues of TBZ in/on sweet potatoes grown from seed pieces treated at 1x exceeded the established 0.2 ppm tolerance.

In response HED's review, Merck has submitted supplemental data (1995, MRIDs 43531002 and 43547601) from the original sweet potatoes field trials. With regards to the over tolerance residues (0.021 and 0.027 ppm) noted in two samples from the original study, the registrant indicated that the sensitivity of the spectrofluorometric method (Method S.A.P 500-P-021) used to originally analyze samples was insufficient to adequately determine residues of TBZ at levels ≤0.02 ppm. The method LOQ and LOD were 0.05 and 0.01 ppm, respectively.

In order to better determine residues of TBZ in mature sweet potatoes grown from treated seed pieces, samples from the original sweet potato field trials were reanalyzed using an improved HPLC/fluorometric detection method (Method M-046), which is discussed above in the Residue Analytical Methods section. The validated LOQ for this method is 0.005 ppm and the estimated LOD is 0.0025 ppm for residues of TBZ in/on sweet potatoes. In addition, selected samples were also analyzed for residues of BNZ (free and conjugated) using Method M-048, which has a LOQ of 0.01 ppm and a LOD of 0.007 ppm for BNZ in/on sweet potatoes. Prior to the second set of sample analyses using the newer methods, samples of treated sweet potatoes were held in storage at ≤-23°C for approximately 52 months. Results of these analyses are presented in Table 4, along with data from the original analyses. Apparent residues of TBZ were <0.005 ppm in/on 5 control samples and 0.005-0.008 ppm in/on the remaining 11 control samples. Apparent residues of BNZ in/on the single control analyzed were <0.007 ppm. Adequate sample

calculations, raw data, and representative chromatograms were provided.

Residues of TBZ were <0.005-0.015 ppm in or on 16 treated samples, and residues of BNZ were <0.007 ppm in/on the four treated samples analyzed. The combined residues of TBZ and BNZ (free and conjugated) were <0.012-<0.022 ppm.

As with potatoes, the registrant requested that HED waive requirements for determining BNZ (free and conjugated) in/on sweet potatoes and argued that TBZ *per se* should be considered the only residue of concern in sweet potatoes. To support their position, the registrant cited the BNZ residue data from sweet potato samples treated at 1x and the published reports (discussed above) indicating that TBZ is not significantly metabolized in potatoes treated post-harvest.

Although HED has concluded that residues of BNZ are unlikely to contribute significantly to total TBZ residues in/on potatoes, the situation for sweet potatoes is different in that residues in/on sweet potatoes are the result of a pre-planting application and data from the metabolism study on sugar beets and the confined rotational crop study indicate that BNZ (free and conjugated) is present in root crops. Accordingly, data are required for residues of both TBZ and BNZ (free and conjugated) in/on sweet potatoes.

The available sweet potato residue data are adequate pending submission of acceptable storage stability data (See conclusion 2c). Residues of TBZ were <0.005-0.015 ppm in/on mature sweet potatoes grown from seed roots treated with TBZ as a 2 minute dip at 0.24 lb ai/7.5 gal. Residues of BNZ (free and conjugated) were non-detectable (<0.007 ppm), and the combined residues of TBZ and BNZ were <0.012-<0.022 ppm. As the maximum combined residues may exceed the established 0.02 ppm tolerance, the tolerance for residues in/on sweet potatoes should be increased to 0.04 ppm. The tolerance of TBZ residues in/on sweet potatoes will be reassessed at the time of the TBZ RED issuance.

Table 4. Residues of TBZ and BNZ (free and conjugated) in/on mature sweet potatoes grown from seed pieces dipped for 2 minutes in TBZ (3.8 lb/gal FlC) at 0.24 lb ai/ 7.5 gal (1x).

Location	Dip Application Rate (lb ai/7.5 gal)	PHI [a] (days)	Residues (ppm)[b]			
			1st analysis [c]	2nd analysis [d]		
			TBZ	TBZ	BNZ	Combined [e]
Winton, CA	0.24	152	0.021, 0.020	0.015	<0.007	<0.022
			0.019, 0.018	0.015	NA [f]	<0.022
			0.013, 0.013	0.011, 0.010	NA	<0.018
			0.011, 0.012	0.010	NA	<0.017
Meigs, GA	0.24	125	0.027, 0.014	0.006	<0.007	<0.013
			0.008, 0.007	0.006	NA	<0.014
			0.006, 0.006	<0.005	NA	<0.013
			0.006, 0.006	<0.005	NA	<0.012
Port Barre, LA	0.24	146	0.008, 0.009	0.005	<0.007	<0.012
			0.008, 0.008	<0.005	NA	<0.012
			0.008, 0.008	<0.005	NA	<0.012
			0.007, 0.008	<0.005	NA	<0.012
Fremont, NC	0.24	122	0.006, 0.007	<0.005	NA	<0.012
			0.006, 0.006	<0.005	NA	<0.012
			0.008, 0.008	<0.005	NA	<0.012
			0.012, 0.007	<0.005	<0.007	<0.012

[a] Days after application.

[b] Expressed in terms of each analyte.

[c] Samples were originally analyzed in duplicate only for residues of TBZ using Merck Method SAP 500-P-021 after 23-24 months of frozen storage.

[d] Samples were analyzed for residues of TBZ using Merck Method M-046, and selected samples were analyzed for residues of BNZ (free and conjugated) using Method M-048. Samples were stored frozen for up to 52 months prior to the second analysis.

[e] Combined residues of TBZ and BNZ; where residue values are unavailable for BNZ, a level of <0.007 ppm was used.

[f] NA = sample not analyzed.

Magnitude of the Residue in Processed Food/Feed

Potatoes

A tolerance of 30 ppm has been established for residues of TBZ in potato processing waste (pre- and post-harvest) [40 CFR §186.5550(a)].

A potato processing study was submitted by Merck in conjunction with the original potato residue studies and was reviewed by HED (J. Abbotts, 8/3/93). Residues of TBZ *per se* were determined in potato flakes, chips, and wet and dry peel processed from unwashed potato tubers bearing residues of TBZ at 6.5 ppm. Residues of TBZ *per se* did not concentrate in potato flakes, chips, and wet peel, but concentrated by 16.6x in dry peel. Residue data for BNZ were not provided.

HED concluded that the potato processing study was inadequate because residues of BNZ (free and conjugated) were not determined and because data supporting the stability of TBZ in potatoes over the 20-month storage interval were not provided.

In its current response (1995,MRID 43547601), Merck has provided supporting storage stability data indicating that TBZ and BNZ are stable in whole potatoes and wet peel at ≤-20°C for at least 27 months. In addition, the requirement for residue data on BNZ (free and conjugated) in potato processed commodities is waived as HED has concluded that BNZ is unlikely to contribute significantly to total TBZ residues in/on potatoes treated post-harvest.

The available potato processing study is adequate. Although residues of TBZ concentrated by 16.6x in potato dry peel, this commodity is no longer listed (Table 1, OPPTS Guideline 860.1000) as a regulated processed commodity of potatoes. Therefore, separate tolerances for potato processed commodities are not required, and the current tolerance should be revoked.

AGENCY MEMORANDA CITED IN THIS DOCUMENT

CBRS No.	None
DP Barcode:	None
Subject:	Thiabendazole Livestock (Goat and Poultry) Metabolism. The Metabolism Committee Meeting Held on February 12, 1992.
From:	L. Cheng
To:	Metabolism Committee, HED
Dated:	2/14/92
MRID(s):	None

CBRS No. 8192
DP Barcode: D165718
Subject: Thiabendazole Phase V Review. Metabolism Studies: Wheat, Soybean, and Sugar Beet.
From: L. Cheng
To: F. Rubis
Dated: 3/11/92
MRID(s): 41872901 through 41872903

CBRS No. 11601
DP Barcode: D189323
Subject: Thiabendazole, Reregistration. Magnitude of the Residue in Sweet Potato, Potato, and Potato Processed Commodities.
From: J. Abbotts
To: J. Ellenberger/C. Giles-Parker
Dated: 8/3/93
MRID(s): 442660301 and 42660302

CBRS No. 11161
DP Barcode: D186572
Subject: Thiabendazole. Magnitude of the Residue Field Trials with Mushrooms.
From: D. Miller
To: F. Rubis.
Dated: 11/22/93
MRID(s): 42598901

MASTER RECORD IDENTIFICATION NUMBERS

The citations for the MRID documents used in this review are presented below.

43531001 Johnson, N. (1995) Merck Responses to EPA Reviews of Thiabendazole--Magnitude of Residue Field Trials with Mushrooms: Lab Project Number: 618-360-R/11161. Unpublished study prepared by Merck & Co., Inc. 28 p.

43531002 Johnson, N. (1995) Merck Responses to EPA Reviews of Thiabendazole--Magnitude of Residue in Sweet Potato, Potato, and Potato Processed Fractions: Lab Project Number: 618-360-R/11601. Unpublished study prepared by Merck & Co.,Inc. 75 p.

43547601 Norton, J. (1995) The Determination of the Presence and Magnitude of Residues of the Fungicide Thiabendazole in Sweet Potatoes Grown from Seed Roots Treated with MERTECT 340-F: Amended Report: Lab Project Number: 618-360-92851: 001-90-3037R: ASA 90 NC01. Unpublished study prepared by Merck Research Labs. 499 p.