Apple Pomace (Partial Review)

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PP#9F2274/FAP#9H5241: Thiophanate methyl in Sugar cane, Pineapples, Almonds, Apples, Beans, Peanuts, Soybeans, and Sugarbeets. Evaluation of analytical method and residue data, and Amendment of 2/1/80.

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The Pennwalt Corporation proposes tolerances for residues of the fungicide thiophanate-methyl, dimethyl[(1,2-phenylene)bis(iminocarbonothioyl)]bis [carbamate], its oxygen analog dimethyl-4,4'-o-phenylene bis(allophanate), and its benzimidazole-containing metabolites (calculated as thiophanate-methyl) in or on the following commodities.

Almond (nuts)	0.2 ppm
Almond hulls	1.0 ppm
Apples (pre-and post-harvest)	7.0 ppm
Beans (snap and dry)	2.0 ppm
Bean vine forage and hay	50.0 ppm
Peanuts	0.2 ppm
Peanuts hulls	2.0 ppm
Peanut forage and hay	15.0 ppm
Soybeans	0.2 ppm
Sugarbeet roots	0.2 ppm
Sugarbeet tops	15.0 ppm
Milk; Eggs; meat, fat, and meat by-products of livestock	0.1 ppm
Liver of poultry	0.2 ppm
Kidney of cattle	0.2 ppm
Liver of cattle	0.5 ppm
Apple pomace, dried (FAP)	70.0 ppm
Sugar Cane	0.1 ppm
Pineapple	0.1 ppm

Tolerances are established for thiophanate-methyl on stone fruits at 15 ppm, strawberries at 5 ppm, and bananas at 2 ppm (§180.371). Temporary tolerances are pending on a number of crops in PP#0G2289.

Conclusions

1. The nature of the residue in plants and animals is adequately understood. The significant components of the residue in plants are the parent compound, thiophanate methyl, and its metabolites: the TM oxygen analog (allophanate); and, methyl-2-benzimidazole carbamate (MBC). The significant components of residues in eggs, milk, and meat are the parent compound, TM, and its metabolites: MBC; hydroxylated MBC; allophanate; and conjugated forms of MBC and hydroxy MBC. The analytical methods are capable of determining the bound and free residue components of plants and animals.

2a. Adequate analytical methods are available for residue determinations in nuts, fruits, and vegetables. However, method trials will be necessary to determine if the methods are adequate for enforcement purposes.

2b. No validation data are submitted for the parent compound, TM, in eggs, meat, and milk. Such data are necessary to determine the methods' adequacy for enforcement.

3a. Residues in or on beans (dry or succulent) and bean forage and hay are not likely to exceed the proposed tolerances.

3b. Residues in or on almonds and almond hulls are not likely to exceed the proposed tolerances.

3c. Residues in or on apples and its by-products (juice, jellies) and apple pomace are not likely to exceed the proposed tolerances. However, the proposed 70 ppm tolerance for apple pomace is excessive. A level of 40 ppm is more appropriate.

3d. Residues in or on sugarbeet roots and its by-products (sugar, pulp) or sugarbeet tops are not likely to exceed the proposed tolerances.

3e. Residues in or on peanuts and its by-products (meal, oil, soapstock), peanut hulls, peanut forage and hay are not likely to exceed the proposed tolerances.

3f. Residues in soybeans or its by-products (meal, oil, soapstock) are not likely to exceed the proposed tolerance.

3g. A tolerance to cover residues in soybean forage and hay is necessary and should be proposed. As an alternative, feeding restrictions on the label would remove the need for a tolerance.

3h. Residues in sugar cane or its by-products (sugar, molasses, bagasse) are not likely to exceed the proposed tolerance. No residue data are submitted which show the presence or absence of residues in the forage. Such data are necessary. If residues occur in the forage and at levels greater than those in the sugar cane, then a tolerance will be necessary to cover residues in the forage. Alternatively, label restrictions on the feed use of the forage would remove the need for a tolerance on the forage.

3i. The pineapple residue data are not adequately indentified. Specifically, samples PI4 and PI6 need to be more fully identified (i.e., which residue levels are associated with fruit, rind, and leaves). These data are needed in order to properly evaluate the proposed use and the tolerance. Additionally, if residues are found in the fruit, then a processing study will be necessary to show if residues are concentrated in the processing fractions (i.e., juice and bran).

4. Residues of thiophanate-methyl and its metabolites are likely to occur in eggs, milk, meat, fat, and meat by-products of livestock [§180.6(a)(1)]. The proposed tolerance levels are not adequate and generally will not cover the residues likely to occur. The following tolerance levels are appropriate.

Milk; Liver of swine and horse	1.0 ppm
Liver of cattle, goats, and sheep	2.5 ppm
Kidney of cattle, goats, and sheep	0.2 ppm
Eggs; Meat, fat, and meat by-products of livestock (except liver and kidney)	0.1 ppm

Recommendation

We recommend against the proposed tolerances. A favorable recommendation is contingent upon the resolution of questions raised in Conclusions 2, 3(c), 3(g), 3(h), 3(i), and 4.

DETAILED CONSIDERATIONS

Formulation

Thiophanate-methyl is formulated as TOPSIN®M, a wettable powder containing 72.9% active ingredient (a.i.).

[redacted] The impurities are not likely to be a residue problem.

The formulation's inert ingredients are cleared for use under §180.1001.

Proposed Use

Aerial or ground applications are permitted to control fungi in various crops. The various uses are noted below.

ALMONDS - BROWN ROT BLOSSOM BLIGHT (Monilinia sp.) - Apply 1.5 to 2.0 pounds of TOPSIN M per acre (1.1-1.5 lb. a.i./A) in sufficient water for thorough coverage at early pink bud and early petal fall. For aerial or concentrate sprays, use an equivalent amount per acre in an amount of water appropriate for the application equipment.

APPLES - SCAB (Venturia sp.), POWDERY MILDEW (Podosphaera sp.), SOOTY BLOTCH (Gloeodes sp.), FLY SPECK (Microthyriella sp.), BITTER ROT (Gloeosporium sp.), and BLACK ROT (Physalospora sp.)- Apply 1.0 to 1.5 pounds of TOPSIN M per acre (0.7-1.1 lb. a.i./A) in sufficient water for thorough coverage at 5 to 10 day intervals from green tip through petal fall; continue at 7 to 14 day intervals in cover sprays.

NOTE: For control of APPLE diseases in the Southeastern States of Florida, Georgia, South Carolina, North Carolina, and Alabama, use 3 to 4 pounds of TOPSIN M per acre (2.2-2.9 lb. a.i./A).

APPLES - POST-HARVEST FRUIT ROTS (Botrytis sp., Penicillium spp., and Gloeosporium sp.) - Dip or spray fruit thoroughly as soon as possible after harvest; use 8 to 16 ounces (5.8-11.7 oz. a.i.) of TOPSIN M per 100 gallons of water (equal to 420 to 840 ppm a.i.). Do not dip for more than 2 minutes. Double the concentration of TOPSIN M when incorporated in wax and applied in flow-through sprays to the fruit.

BEANS - WHITE ROT (Sclerotinina sp.) and GRAY MOLD (Botrytis sp.) - Apply 1.5 to 2.0 pounds (1.1-1.5 lb. a.i.) of TOPSIN M per acre in sufficient water for thorough coverage once at 50% to 70% bloom. Or, apply 1.0 to 1.5 pounds (0.7-1.1 lb. a.i.) of TOPSIN M per acre twice with the first application when 10% to 30% of the plants have an open blossom and a second application 4 to 7 days later or at peak bloom. Do not apply to snap or dry beans within 14 days of harvest, or to lima beans within 28 days of harvest.

PEANUTS - LEAF SPOT (Cercospora spp.) - Apply 8 ounces of TOPSIN M per acre (5.8 oz. a.i./A) in sufficient water for thorough coverage. Begin applications 35 days after planting or when disease first appears and repeat at 14 to 21 day intervals as needed. Use the 14 day interval under severe disease conditions. Do not apply within 14 days of harvest.

PINEAPPLE - BUTT ROT (Thielaviopsis sp.) - Apply 4 to 16 ounces (2.9-11.7 oz. a.i.) of TOPSIN M per 100 gallons of water as a per-plant dip treatment of seed pieces. Immerse seed pieces to provide thorough coverage; remove and allow to drain.

SOYBEANS - ANTHRACNOSE (Colletotrichum sp.), BROWN LEAF SPOT (Septoria sp.), FROG-EYE LEAF SPOT (Cercospora sp.), PURPLE SEED STAIN (Cercospora sp.), and POD AND STEM BLIGHT (Diaporthe sp. and the imperfect stage, Phomopsis sp.) - Apply 8 to 16 ounces (5.8-11.7 oz. a.i.) of TOPSIN M per acre in sufficient water for thorough coverage. Start applications when pods are 1/8 inch to 1/4 inch in length and repeat at 10 to 14 day intervals. Do not make more than 3 applications per year. Use the high rate under severe disease conditions.

SUGAR BEETS - LEAF SPOT (Cercospora sp.) - Apply 6 to 8 ounces (4.4-5.8 oz. a.i.) of TOPSIN M per acre in sufficient water for thorough coverage. Begin applications when disease first appears and repeat at 14-21 day intervals as needed. Do not apply within 21 days of harvest.

SUGAR CANE - PINEAPPLE DISEASE (Thielaviopsis sp. or Ceratocystis sp.) - Apply TOPSIN M to cut seed pieces either as a cold or hot dip.

Cold Dip - use 8 ounces TOPSIN M (5.8 oz. act) per 100 gallons of water (1:1,600) to 1 pound per 100 gallons (1:800). Immerse seed pieces to provide thorough coverage; remove and allow to drain.

Hot Dip - Use 4 ounces TOPSIN M (2.9 oz. act) per 100 gallons of water (1:3,200) to 8 ounces per 100 gallons of water (1:1,600). Maintain temperature of dip at 52°C and soak seed pieces for 20 minutes; remove and allow to drain.

Do not use treated seed pieces for food, feed, or fodder.

Nature of the Residue

We have previously considered the metabolism and degradation of thiophanate-methyl (TM) in plants, animals, and soils (Menzies, "Metabolism of Pesticides", PPs 2G1249, 5F1589, 7G1938). In plants (apples, beans, grapes), TM is absorbed, translocated, and metabolized. Plant residues consist of the parent compound, TM, and its metabolites: the dioxygen analogue of TM, [dimethyl 4,4'-o-phenylene bis (allophanate)]; methyl 2-benzimidazole carbamate (MBC), and traces of components containing the benzimidazole moiety.

A study with TM and soybeans was submitted in this petition (PP#9F2274). Soybean plants were sprayed with radiolabelled C^{14}-TM. Samples of pods and leaves were examined for residues at 1 week and 2 weeks after treatment. Examinations were carried out by analyses with liquid scintillation counting techniques (LSC) and high performance liquid chromatography (HPLC).

The soybean plant residues consisted of TM (73-86%) and its metabolites: 1-(3-methoxycarbonylthioureido)-2-(3-methoxycarbonylureido)benzene, DX-105, <1.0%; the dioxygen analog of TM, [dimethyl 4,4'-o-phenylene bis (allophanate)], FH-432, (1-4%);methyl 2-benzimidazolecarbamate, MBC, (9-15%).

In soil TM decreased to less than one-half the initial dose within 2 days after application. TM had almost completely disappeared within 7 days. The soil residue consisted primarily of the parent compound, TM, and MBC.

In animals (mice, rat, sheep, dog) TM is metabolized and excreted. The metabolic residue consists of TM and its metabolites: MBC; hydroxylated MBC; allophanate 2-aminobenzimidazole (2-AB), 5-OH-(2-AB); the glucuronides of hydroxy MBC, MBC, 2-AB, and hydroxy 2-AB.

Studies were submitted with this petition (PP#9F2274) which entailed the feeding of radiolabelled (ring label) C^{14}-thiophanate-methyl (TM) at a level of 15.5 ppm to lactating cows. About 83-89% of the total daily dose was excreted in urine, feces, and milk. Residues were also distributed throughout the body.

The residues in milk consisted of the parent compound, TM, and about 85% of the residue was conjugated (about 2/3 of residue) and free forms (about 1/3) of the following metabolites; MBC, 9.8%; 4-hydroxy-MBC (6.8%); 5-hydroxy-MBC, 47.6%; 4-hydroxy-TM, 13.4%; and other minor compounds, 7.4% di-oxygen analog of TM (allophanate, or FH-432), hydroxylated FH-432, and 2-aminobenzimidazole (2-AB).

Poultry feeding studies were also submitted in this petition. Laying hens were fed a combination of radiolabelled C^{14}-TM and unlabelled TM for periods of 10 and 30 days. As in previous animal studies, the major portion of ingested residues was excreted.

Residues were also excreted in the eggs and reached a plateau at 3 days after the feeding began. Residues were also distributed throughout the tissues. Residues in the eggs and tissues consisted of the parent, TM, and its bound and free metabolites: MBC; 5-OH-MBC, and 5-OH-MBC-sulfate.

Residues in tissues of large animals (cows, sheep) were not characterized. However, the metabolism studies for cows and sheep as well as the small animals show similar metabolic pictures as reflected in characterization of residues in milk, eggs, urine, feces, as well as tissues of rats. It is therefore reasonable to conclude that the deposition pattern noted in milk, urine, and feces reflects the components likely to occur in tissues.

The nature of the residue in animals and plants has been adequately delineated. The significant components of the residues are the parent compound, thiophanate methyl (TM), its oxygen analog (allophanate), and its benzimidazole-containing metabolites.

Generally, a metabolism study with radiolabelled TM and a root crop would be necessary. However, the soil study showed the residue components in soils to be similar to those in plants, and our concern is the uptake of soil residues by the root. Thus, the absence of a root crop metabolism study does not pose a problem. As a result, the nature of the residue in plants, in general, is adequately reflected in the available plant metabolism studies.

Residue Storage Stability

Crops (apples, beans, onions, cherries, plums, apricots, nectarines, strawberries) were fortified with the TM formulation and kept frozen. Samples were then analyzed for residues of TM and MBC at periods of 1 day to 3 years. No significant decrease in residues were noted during the storage period. Therefore, we conclude that frozen storage of samples containing residues of thiophanate methyl does not affect the level of residues in the samples.

Analytical Methods

Thiophanate-Methyl, MBC, and Allophanate - (Generally applicable to fruits and vegetables)

A sample is extracted by blending with acetone, filtering, and evaporation of the solvent. (For nutmeats, a mixture of methanol and hydrochloric acid is used. For soybeans, only methanol is used). The aqueous solution remaining after evaporation is adjusted to pH 6.5-7.0 and extracted with methylene chloride which is evaporated. The residue is treated with acetic acid and cupric acetate and heated for one hour. (This treatment converts the parent, TM, to the metabolite MBC.)

The treated solution is diluted with hydrochloric acid and washed with heptane which is discarded. The aqueous solution is extracted with chloroform. (The chloroform extracts contain the metabolite allophanate.)

The pH of the aqueous phase is adjusted to 6.5-7.0 and extracted with chloroform. (The aqueous layer is discarded.) The residues are extracted into sodium hydroxide solution, and the pH is adusted to 6.5-7.0. The residues are extracted into chloroform, washed with water, and extracted into sulfuric acid solution.

The acid solution is examined spectrophotometrically in the ultraviolet region. The residues of MBC are quantitated by comparison with an MBC standard curve. The results are expressed as thiophanate methyl (TM).

TM and MBC may be determined separately by appropriate modifications included in the method.

Allophanate Determination

The chloroform extracts which contain allophanate residues (FH-432) are cleaned up on a florisil column, and allophanate is eluted with ethyl acetate and an ethyl acetate: methanol mixture. Allophanate residues are determined by high performance liquid chromatography (HPLC) using an ultraviolet detection system.

A method similar to the above method is provided for the analysis of TM and MBC. The extraction and clean-up procedures are essentially the same, but the determinative steps differ. TM is coverted to MBC, and a color is developed with bromcresol purple. The absorbance of the solution is measured spectrophotometrically, and the quantity of MBC is determined by reference to a standard curve. Residues of MBC are expressed in terms of thiophanate methyl (TM).

An analytical method is submitted for the determination of the TH metabolite DX-105, [1-(3-methoxycarbonyl-2-thioureido)-2-(3-methoxycarbonylureido)benzene]. DX-105 is a transitory intermediate in the formation of MBC and allophanate (FH-432). DX-105 is believed to be converted to MBC during normal residue analysis for TH and MBC.

A sample is extracted by blending with acetone, filtering, and evaporation of the acetone. The remaining aqueous extract is acidified with hydrochloric acid and washed with petroleum ether which is discarded. The aqueous phase is then extracted with methylene chloride. (The aqueous phase is discarded.)

Residues in the methylene chloride are extracted into dilute sodium hydroxide solution. The pH is adjusted to 6.5-7.0, and the residues are extracted into methylene chloride which is filtered and concentrated. The residues in the concentrate are determined by HPLC.

Milk Analysis

The following procedure determines the metabolites MBC and 5-OH-MBC, (methyl-5-hydroxy-2-benzimidazolecarbamate). The free and conjugated components are determined. However, the method is not validated for TH.

A sample is hydrolyzed by refluxing with phosphoric acid (frees conjugated compounds), cooled, and washed with hexane which is discarded. The remaining aqueous phase is brought to a pH of 6.5-7.0 and extracted with ethyl acetate. (The aqueous phase is descarded.)

The ethyl acetate phase is acidified with acetic acid and concentrated. Residues are extracted into hydrochloric acid. This phase is adjusted to pH 6.5-6.8, and residues are extracted into ethyl acetate which is acidified and concentrated. The residues are determined by HPLC using an ultraviolet detector.

Egg Analysis

This procedure determines the bound and free metabolites, MBC and 5-OH-MBC. However, the method has not been validated for TH.

A sample is extracted by blending with methanol. The methanol extract is diluted with phosphoric acid and washed with hexane. The acidic methanol containing the residues is heated (frees conjugated components), cooled, and adjusted to pH 6.7-7.0. The residues are extracted with an ethyl acetate/chloroform mixture. The residues are next extracted into dilute hydrochloric acid. The pH of the extract is adjusted to 6.7-7.0.

The residues are extracted into ethyl acetate which is dried and evaporated. The residue is taken up with methanol and determined by high performance liquid chromatography (HPLC).

Animal Tissue Analysis

The method determines the bound and free metabolites MBC and 5-OH-MBC. However, the method is not validated for the parent compound TM.

A sample is extracted by blending with hydrochloric acid in methanol. The extract is washed with petroleum ether and partitioned into hydrochloric acid. The acid phase is refluxed with heat which hydrolyzes the bound components. The solution is washed with chloroform, and the pH is adjusted to 7.0. The solution is then extracted with a mixture of ethyl acetate/chloroform which is dried over sodium sulfate and concentrated.

The residues are extracted into hydrochloric acid which is adjusted to pH 7.0. The residues are again extracted into an ethyl acetate: chloroform mixture which is evaporated. The residues are taken up in methanol and determined by HPLC.

Methods Validation Data

The crops (almonds, apples, pineapples, sugar cane, beans, peanuts, soybeans, sugarbeets), their forages, and by-products had <0.02-<0.2 ppm TM or MBC-equivalent residues when residues were determined by the ultraviolet procedure. Untreated (control) samples of the various commodities were fortified with TM or MBC at levels of 0.05-10 ppm. Recoveries were 50-130%.

Control samples of the various crops had <0.05 ppm allophanate (FH-432) equivalent residues using the high performance liquid chromatography (HPLC) procedure. control samples were fortified with allophanate at levels of 0.05-1.0 ppm. Recoveries were generally 56-100% (2 aberrant values of 26% and 44% were also noted.).

Thiophanate-methyl (TM) and MBC were also determined using the colorimetric procedure. Control samples of apples, peanuts, and sugarbeets had <0.02-<0.1 ppm TM or MBC-equivalent residues. Control samples of these crops were fortified at levels of 0.05-10 ppm with TM and MBC. Recoveries were 57-120%.

The method for OX-105 was validated for apples, sugarbeets, and peaches. Control samples were fortified with OX-105 at levels of 0.05-1.0 ppm. Recoveries were 47-98%.

Control egg samples were fortified with MBC and 5-OH-MBC at levels of 0.05-0.20 ppm Recoveries were 60-103%.

Chicken thigh control samples were fortified with MBC and 5-OH-MBC at levels of 0.05 ppm and 0.20 ppm. Recoveries were 80-93%.

The methods for eggs, milk, and meat are not validated for the parent compound, TM. Validation data for TM in eggs, meat, and milk are necessary and should be submitted.

A successful method trial has been performed on strawberries at levels of 2.5 ppm and 5.0 ppm with thiophanate methyl and MBC (PP#5F1573, memo 5/7/75, R. Watts). The average value for untreated samples was 0.25 ppm. Thus, the method's sensitivity with strawberries is, at best, 0.25 ppm.

For specificity, thin layer chromatography (TLC) and liquid chromatography (HPLC) procedures are available.

The proposed tolerances are in terms of TM, its oxygen analog, allophanate, and its benzimidazole containing metabolites. Should the determination of benzimidazole-containing metabolites beyond MBC be required, then methods which determine such residues have been developed in connection with benomyl [JAOAC 54, 1399 (1971); J. Ag. & Fd. Chem., 21, 368(1973)].

The present tolerance proposals contain residue levels which are below the sensitivity of the UV method (0.25 ppm) above as tested by EPA. (For example, almonds, peanuts, and beans at 0.2 ppm, as well as milk, eggs, and meat at levels of 0.1-0.5 ppm). As a result, method trials at these levels with representative crops and eggs and meat will be necessary. The residue components to be tested will be determined when the additional information that we are requesting is submitted.

Residue Data

Samples were collected from crops of green and dry beans which were grown in Washington, Oregon, New York, California, Pennsylvania, and North Dakota.

Snap Beans

Crops were treated in the proposed manner with single applications (ground or air) at rates of 0.7-2.8 lb. a.i./A (up to 1.9X maximum proposed rate) and harvested at intervals of 0-42 days after treatment (PHI). Residues in the beans were N.D. (none detectable, <0.05 ppm) -3.7 ppm at PHI's (1.1-1.5 lb. a.i./A at a PHI of 14 days), residues in beans were <0.05-0.91 ppm.

Snap beans treated with two ground applications at rates of 0.7-1.4 a.i./A (proposed, 0.7-1.1 lb. a.i./A) had residues of <0.05-0.34 ppm at PHI's of 0-15 days.

Snap bean foliage had residues of 13-162 ppm (0-day), 1-25 ppm (7 days), 8 ppm (9 days), and 0.7-16.5 ppm (14-day PHI) due to a single ground application at rates of 0.7 or 1.4 lb. a.i./A.

When treated with two applications at 0.7 and 1.4 lb. a.i./A, snap bean foliage had residues of 0.1-19 ppm at PHI's of 0-15 days.

Dry Beans

Samples were obtained from crops which had received 2 applications at a rate of 1.4 lb. a.i./A. Residues in beans were 0.64 ppm at 7 days and <0.05 ppm at 41 days.

Pinto Beans

Samples of beans were obtained from crops which had received one or two applications at rates of 0.7 and 1.4 lb. a.i./A. Residues at 0-day due to 2 applications of 0.7 lb. a.i./A were 5.24 ppm. Residues at 7 days were 0.37 ppm, and 0.14 ppm at 14 days. Residues at 0-day due to the single application at 1.4 lb. a.i./A were 4.13 ppm. Residues at 7 days were 0.55 ppm.

Navy Beans

Samples of beans and forage were obtained from crops which had received 2 applications at 1.4 lb. a.i./A and one at 2.8 lb. a.i./A. The beans had no detectable residues (N.D., <0.05 ppm) at either 15 or 30 days from the 2 applications; however, the forage had 20.3 ppm at 15 days and 0.5 ppm at 30 days. From the single 2.8 lb. a.i./A rate, the beans had 0.13 ppm at 15 days, and the forage had 17.9 ppm (15 days) and 1.8 ppm (30 days).

Lima Beans

Samples were collected from crops which had received one application at 1.4 lb. a.i./A and 2 applications at rates of 0.7, 1.4, and 2.8 lb. a.i./A. From the single application, the beans had residues of 0.54 ppm at 14 days. Residues in beans were 0.21 ppm at 14 days due to 2 applications at 0.7 lb. a.i./A.

Residues in the beans were 0.60 ppm at 14 days and 7.0 ppm in the forage at 28 days due to the 1.4 lb. a.i/A rate. Residues in the forage at 0-day were 72.8 ppm, 52.9 ppm at 7 days, and 34.3 ppm at 14 days. Residues due to the 2.8 lb. a.i./A rate were 0.8 ppm in the beans and 45 ppm in the forage at the proposed 28 day PHI. Residues in the forage and beans were higher at shorter PHI's and decreased with time.

Residues of thiophanate methyl and its metabolites in or on beans (dry or succulent) or its forage and hay are not likely to exceed the proposed tolerances of 2.0 ppm and 50 ppm, respectively. The levels proposed may appear excessive; however, such levels will compensate for variations expected in the residues.

The data for the forages are sufficient to reflect residue levels in the hays. Therefore, no additional residue data are necessary for the hays.

Almonds

Samples were obtained from crops in California which had been treated at rates of 4.2 and 8.6 oz. a.i./100 gallons (up to 1.2X maximum rate). No residues were noted in either the nutmeats (<0.05 ppm) or the hulls (<0.1 ppm) from either rate and at PHI's of 215 and 232 days.

Four hull and four nut samples, representing two varieties, were submitted as residue data. In an earlier review of a temporary tolerance proposal (PP7G1938, memo 11/16/77, M. Nelson), we indicated that such data were adequate for a temporary tolerance, but additional data would be necessary for a permanent tolerance. Additionally, we used data for pecans (which also showed the absence of residues in nuts when used in a similar manner) to support the conclusion that residues in almonds, if present, would be below the limits of detection (i.e., less than 0.1 ppm. See PP#5G1886 for pecan data.).

In view of the foregoing, it is reasonable to expect that residues, if present, in almonds would be below the analytical sensitivity of the method (<0.1 ppm). Therefore, the available data are adequate to show if residues are present in almonds.

Residues of TM in or on almonds and almond hulls are not likely to exceed the proposed tolerances.

Apples

Samples of apples were obtained from orchards in California, Washington, Pennsylvania, North Carolina, Virginia, Georgia, New Jersey, Michigan, Oregon, and New York. The orchards had received air or ground applications as proposed at proposed and exaggerated rates. Pre-harvest treatments alone (proposed: multiple applications at 2.9-4.4 oz. a.i./100 gallons water; for Florida, Georgia, South Carolina, North Carolina, and Alabama, use 8.8-11.7 oz. a.i./100 gal.)

Samples were obtained form California, Washington, Pennsylvania, Virginia, New Jersey, Michigan, Oregon, and New York which had received 1-17 applications at rates up through 5.4X proposed and harvested at 0-120 days after the last treatment. Overall, residues were <0.05-4.02 ppm. From the proposed rates, residues were 0.30-1.44 ppm at PHI's of 0-4 days. At PHI's of 5 days and greater, residues were 0.10-0.32 ppm.

Samples were obtained form North Carolina and Georgia which had received 11 applications at rates of 1X-1.4X maximum proposed and harvested at 0-29 days after the last treatment (PHI). Residues at 0-day were 4.5 ppm; at 14 days, 2.4 ppm; and 0.14-0.45 ppm at 29 days due to the proposed rates.

Post-Harvest treatments alone (proposed: dip or spray at rates equivalent to 420-840 ppm a.i.; double concentration when incorporated in wax and applied in flow-through sprays).

Samples were obtained from apples treated by aqueous spray, aqueous dip, or aqueous drench with solution concentrations of 840-5,000 ppm. Residues were 2.1 ppm due to the maximum proposed concentration. Overall, residueswere 2.1-4.1 ppm.

Samples were obtained from apples treated by machine wax, hand wax, or wax spray at 2,000 ppm or a wax dip at 5,000 ppm (approximately 3X maximum proposed concentration). Residues due to the 1.2X concentration were 0.31-1.6 ppm. Residues were 0.70-0.94 ppm due to the 3X concentration.

Pre-Harvest plus Post-Harvest treatments

Samples were collected from apples which had received pre-harvest treatments of 11 application at 3.5 oz. a.i./100 gal. and harvested at a PHI of 1 day and a post-harvest immersion treatment on day 2 at a concentration of 1,050 ppm. Residues were 2.26-3.59 ppm.

Apple By-products

Samples of apples which had been treated in the proposed manner were analyzed for residues and processed to juice and pomace. The juice and pomace were analyzed for TM residues. The results showed that residues in whole apples were concentrated in the dehydrated pomace (3.2X-4.0X), but no concentration was noted in the apple juice.

Based on the maximum concentration factor of 4X, a level of 28 ppm (4X 7 ppm in fresh apples) would be expected in dehydrated apple pomace. In order to compensate for variations in concentration factors, we believe a level of 40 ppm would be more appropriate (cf. 16% dry matter in fresh apples versus 89% dry matter in dried pomace which yields a concentration factor of 5.6).

In view of the foregoing, we consider the proposed 70 ppm level for dehydrated apple pomace to be excessive. A tolerance level of 40 ppm is more appropriate and should be proposed.

Residues of thiophanate-methyl in or on apples or apple juice and jellies are not likely to exceed the proposed tolerance (7 ppm) for apples.

Sugar Beets

Samples of roots and tops were collected from crops grown in California, Michigan, Iowa, and Ohio which had received 2-4 applications as proposed at rates of 5.6-11.2 oz. a.i./A (up to 1.9X maximum proposed rate). At the proposed rates, the roots and tops had residues of <0.05 ppm (N.D., none detectable) at 34-67 days after the last treatment. At the 1.4X rate, the roots and tops also had residues of <0.05 ppm at 24-74 days after the last treatment. Residues due to the 1.9X rate were <0.05 ppm in roots and 11.7 ppm in the tops at day-1. At day-15, the roots had <0.14 ppm and the tops had 11.0 ppm. At the proposed 21-day PHI, the roots had <0.05 ppm and the tops had 9.0 ppm. Residues generally decreased slowly with time. At 56 days residues in the tops were 0.4 ppm.

Sugarbeet roots which contained <0.05 ppm TM residues were processed and the fractions were analyzed for TM residues. No detectable residues were noted in the wet or dry pulp or the thick juice. In view of the absence of residues in the thick juice, it is not likely that residues will occur in the sugar fraction.

We conclude that residues of TM in or on sugarbeet roots and tops are not likely to exceed the proposed tolerances.

Peanuts

Samples were obtained from crops in Texas, Georgia, North Carolina, Texas, Alabama and Oklahoma which had been treated as proposed at rates of 5.6-12 oz. a.i./A (up to 2X maximum proposed rate) and harvested at intervals of 0-55 days after treatment (PHI).

Overall residues in the nutmeats were 0.02-0.17 ppm at PHI's of 0.-51 days from 4-12 applications. Residues in shells due to the proposed rate and PHI (5.8 oz. a.i./A and 14 day PHI) were <0.1 ppm (actually 6 applications and 17-day PHI). Maximum residues of 0.17 ppm were due to 12 applications and a 51-day PHI. Residues in nutmeats at 0-day were 0.04 ppm from 6 application at 12 oz. a.i./A (2X).

The shells had residues of 0.12-0.64 ppm due to 4-12 applications at rates of 5.6-12 oz. a.i./A. At approximately the proposed uses (6 applications at 5.6-11.2 oz. a.i./A), the shells (or hulls) had 0.12 ppm TM residues at a 17-day PHI.

The vines had overall residues of 0.16-5.7 ppm (green) and 0.16-2.3 ppm (cured) due to 4-7 applications at 5.6-12.0 oz. a.i./A and PHI's of 9-65 days. At conditions approximating the proposed uses, green vines had a maximum of 5.7 ppm and cured vines had a maximum of 2.3 ppm TM residues.

Peanut Processing Fractions

Nuts which contained 0.02-0.05 ppm TM residues were processed to oil and meal. The refined oil had 0.01-0.03 ppm TM residues and the meal had 0.02-0.03 ppm.

No data are submitted for soapstock. However, because of the low level of residues in the nutmeat and the various fractions analyzed, it is not likely that residues, if any, in the soapstock would be concentrated.

Residues of TM in or on peanuts or its by-products (meal, oil, soapstock) and peanut hulls are not likely to exceed the proposed tolerances.

Residues in peanuts forage or hay are not likely to exceed the proposed tolerance (15 ppm).

Soybeans

Samples of soybeans and soybean foliage were obtained from crops in the major soybean growing regions which had been treated as proposed with 1-3 ground or air applications at rates of 5.6-16.0 oz. a.i./A and harvested at intervals of 14-74 days after the last treatment. (The proposed use is 5.8-11.7 oz. a.i./A when pods are 1/8-1/4 inch long and repeat at 10-14 day intervals. A maximum of 3 applications per year is permitted.)

No detectable residues (<0.05 ppm) were noted in soybeans at any rate.

Soybean By-products - soybean seed which contained no detectable residues (<0.05 ppm) were processed to meal, oil, and soapstock. The meal and oil were analyzed for TM residues. No detectable residues (<0.05 ppm) were noted in meal or refined oil. The absence of residues in the oil or meal precludes residues in the soapstock. Moreover, the data for peanuts in the above discussion support the conclusion that residues, if any, in soybeans would not be concentrated in its by-products.

Soybean foliage - samples of foliage were obtained from crops which had received 2 application at 11.2 oz. a.i./A and harvested at intervals of 0-55 days after treatment. Residues at 0-day were 7.8-16.9 ppm; at 7-days, 0.47-2.3 ppm; at 14-days, 0.08-0.50 ppm; and, no detectable residues (<0.05 ppm) at 55 days.

Residues in soybeans or its by-products (meal, oil, soapstock) are not likely to exceed the proposed tolerance (0.2 ppm) from the proposed use.

A tolerance to cover residues in forage and hay is necessary and should be proposed. Since there is no grazing restriction, the soybeans could be grazed on the day of treatment. At this period a level of about 20 ppm TM could be on the forage.

Sugar Cane

Samples were obtained from crops in Hawaii which were grown from seed pieces treated with hot water dip (400 ppm TM) or cold water dip (800 ppm TM). (The dip concentrations are approximately 2X the proposed rates.) No detectable residues (N.D., <0.05 ppm) were noted in the sugar cane from either treatment at 225 days after treatments and planting.

No data are submitted for the processing fractions (sugar, bagasse, molasses,) or forage. The absence of detectable residues in sugar cane from twice the proposed rate indicates that residues are not likely to occur in sugar, molasses, and bagasse. Moreover, should residues occur, such levels would be less than the level in the sugar cane.

Since the forage of sugar cane may be fed to cattle and sheep, residue data are needed to show the level of residues, if any, in the forage. Additionally, if residues do occur in forage and at levels greater than that in the sugar cane, then a tolerance would be needed to cover such residues.

Alternatively, a label restriction on the feeding of forage or fodder grown from treated sugar cane seed pieces would be sufficient to lessen the liklihood of the livestock ingestion of residues through these sources.

Pineapples

Samples of fruit, rind, and leaves were obtained from crops in Hawaii. The crops were grown from seed pieces which had been treated as proposed and harvested 1.5 years after treatment. No detectable residues (<0.1 ppm) were noted in any samples. (These data were previously submitted and considered in PP#7G1938.)

A second set of data were submitted with this petition (PP#9F2274). Pineapples were grown from seed pieces treated as proposed and harvested at 6 and 22 months. No detectable residues (<0.05 ppm) were noted in fruit, rind, or leaves at 22 months, or two samples at 6 months.

A second set of two samples (samples PI-4 and PI-6) had residue levels of 0.07-0.60 ppm. All levels (except 1 at 0.07 ppm) were 2.5-6 times greater than the proposed 0.1 ppm tolerance. Moreover, it is not known what components (fruit, rind, leaves) that the residue levels represent.

The petitioner should be informed that the samples PI-4 and PI-6 need to be more fully identified. It is necessary to know which residue levels are associated with fruit, rind, and leaves. These data are necessary in order to properly evaluate the proposed use and tolerance.

Since the residue data are inadequate, a valid conclusion on the proposed tolerance is not possible.

If residues are found in the pineapple fruit, then a processing study will be necessary to show if residues are concentrated in the processing fractions.

Livestock Feeding Studies

Cow Feeding Studies

four lactating cows were fed radiolabelled (ring label) C^{14}-thiophanate methyl (C^{14}-TM) equivalent to 15.5 ppm in the diet daily for 11 days. Milk and fecal samples were collected periodically and analyzed for radioactive residues. Following the end of the feeding period, the animals were sacrificed, and tissue samples were collected and analyzed for residues of TM and its metabolites.

Approximately 83-89% of the total daily dosages were excreted: urine, 59-68%; feces, 17-24%; milk, 0.5-0.6%. Residues in milk plateaued at 4-6 days after the onset of feeding, and milk residues were 0.09-0.12 ppm during feeding.

Residues were distributed throughout the body. Tissue residues were: liver, 1.1-1.5 ppm; kidney, 0.4-0.5 ppm; muscle, 0.03-0.05 ppm; fat, 0.03-0.08 ppm.

Another study was submitted in which six lactating cows (cows/group) were fed a combination of radiolabelled C^{14}-TM and unlabelled TM daily at levels equivalent to 15, 45, and 150 ppm for 30 days. Milk samples were collected daily and analyzed for radiolabelled residues. After 30 days, the animals were sacrificed, and tissue samples were collected and analyzed for residues. The following tabulation shows the residue levels from the various feeding levels.

FEEDING LEVELS (PPM)	TOTAL RESIDUES FOUND (PPM TM)				
	MILK	LIVER	KIDNEY	MUSCLE	FAT
15	0.79	1.03	0.05	0.00	0.00
45	2.66	6.69	3.76	0.00	0.00
150	9.91	17.19	11.17	0.00	0.00

Poultry Feeding Studies

Thirty laying hens were fed radiolabelled C^{14}-thiophanate methyl (C^{14}-TM) daily at a level equivalent to 50 ppm in the diet for ten days. Eggs were sampled at periodic intervals and analyzed for residues. The birds were sacrificed at the end of the feeding period, and tissues were analyzed for radioactive residues which were expressed as ppm TM.

In eggs total radioactivity reached a plateau at about day-7 of the study. Maximum residues noted were 0.26 ppm. The total radioactivity levels were determined by acid digestion and liquid scintillation counting techniques. Residues in eggs and tissues were also analyzed chemically by the HPLC method (see Analytical Methods), characterized, and identified by HPLC, thin-layer chromatography (TLC), and liquid scintillation counting (LSC).

The residue in eggs consisted primarily (average, 95%) of TM and its metabolites MBC and 5-hydroxy-MBC.

In tissues, the residues consisted primarily of TM, MBC, 5-OH-MBC, and 5-OH-MBC sulfate. Residue levels in tissues were 0.01 ppm (fat)and 0.04 ppm (breast and leg).

In another study 10 laying hens were fed a combination of unlabelled and radiolabelled C^{14}-TM at doses equivalent to 10 ppm and 50 ppm TM daily for 30 days. Eggs were sampled at regular intervals and analyzed for C^{14}-radioactivity. The birds were sacrificed at the end of the feeding period, and tissue samples were collected and analyzed for C^{14}-activity. Radioactivity found was expressed in terms of TM residues. The results are tabulated below.

FEEDING LEVEL (PPM)	TOTAL RESIDUES FOUND (PPM)				
	EGGS	MUSCLE	FAT	LIVER	KIDNEY
10	0.061-0.081	0.00	0.00	0.180-0.447	0.102-0.196
50	0.171-0.377	0.00	0.00	0.585-1.692	0.421-1.221

Meat, Milk, and Eggs

Apples, apple pomace, almond hulls, beans, bean forage, peanuts, peanut meal, peanut forage and hulls, soybeans, soybean forage, soybean meal, sugar cane forage and molasses, sugarbeets and tops, and pineapple bran may be used as livestock feeds. Considering the various levels of the feed items in the diet and the level of residues expected in each item, maximum levels of residues which could be ingested by livestock can be estimated. The animals and the maximum ingestion levels are as follows. Cattle (20 ppm); non-egg laying poultry (2 ppm); egg laying poultry (0.3 ppm); swine (6 ppm); horses (12 ppm); and sheep and goats (20 ppm).

Through the use of the above ingestion levels and the cattle and poultry feeding studies, the levels of residues likely to occur in eggs, milk, and tissues can be estimated. The various levels are as follows:

Cattle - milk (1.25 ppm), liver (2.75 ppm), kidney (0.25 ppm), muscle and fat (<0.1 ppm).

Poultry - eggs, liver, kidney (≤0.1 ppm)

Swine - liver (0.75 ppm), kidney (≤0.1 ppm), other tissues (≤0.1 ppm)

Horses - liver (1.25 ppm), kidney and other tissues (≤0.1 ppm)

Sheep and Goats - liver (2.75 ppm), kidney (0.25 ppm), other tissues (≤0.1 ppm).

Residues of thiophanate and its metabolites will occur in eggs, milk, meat, fat, and meat by-products of livestock [§180.6(a)(1)]. The proposed tolerance levels are inadequate and will not generally cover the residues likely to occur in eggs, milk, and meat. The following tolerance levels are appropriate.

Milk; liver of swine and horses	1.0 ppm
Liver of cattle, goats, and sheep	2.5 ppm
Kidney of cattle, goats, and sheep	0.2 ppm
Eggs; meat, fat, and meat by-products of livestock (except liver and kidney)	0.1 ppm

Other Considerations

The fungicide benomyl and the fungicide thiophanate methyl have as common residue components metabolites which contain the benzimidazole moiety. This situation is adequately covered in §180.3(d)(10)-Tolerances for Related Pesticide Chemicals.

As a result, no problems are expected because of the establishing of tolerances for thiophanate methyl on crops which have established tolerances for benomyl.

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cc: RF, Circ., A. Smith, Watts, FDA, TOX, EEB, EFB, PP#9F2274/9H5241
RDI: R.S. Quick:7/18/80:R.D. Schmitt:7/21/80