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

JAN 6 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#8E3642. Triadimenol (Baytan or BAY KWG 0519) on Imported Bananas. Evaluation of Analytical Method and Residue Data. MRID #406152-01. RCB #3926.

FROM: Sami Malak, Ph.D., Chemist
Tolerance Petition Section III
Dietary Exposure Branch/DEB
Health Effects Division/HED (TS-769C)

TO: Louis Rossi, PM #21
Fungicide-Herbicide Branch
Registration Division (TS-767)

and

Toxicology Branch
Herbicide-Fungicide Support
Health Effects Division (TS-769C)

THRU: P. V. Errico, Section Head
Tolerance Petition Section III
Dietary Exposure Branch
Health Effects Division (TS-769C)

Presumably, the Mobay Chemical Corporation is requesting the establishment of a permanent tolerance at 0.2 ppm for residues of the fungicide triadimenol (Baytan or BAY KWG 0519), beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol and its metabolites containing the chlorophenoxy and triazole moieties in/on bananas that will be imported to the United States.

Section F included in this petition does not identify the pesticide for which a tolerance is requested. The petitioner

is advised to revise Section F by indicating the chemical name of the parent compound and any metabolites of toxicological concern that ought to be regulated in the tolerance expression for Baytan. It was previously stated (PP#5F3224/FAP#5H5458, M. Firestone, 5/31/85), that in order to be consistent with the tolerance expression for Bayleton established under 40CFR§180.410, 21CFR§193.83, and 21CFR§561.93, Baytan tolerances should be expressed in terms of the combined residues of Baytan and it metabolites containing chlorophenoxy and triazole moieties (expressed as Baytan). However, after careful re-evaluation of the available data for both Bayleton and Baytan, it is our assessment that tolerances for Baytan should be expressed as follows: "The combined residues of the fungicide, beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol, and its butanediol metabolite, 4-(4-chlorophenoxy)-2,2-dimethyl-4-(1H-1,2,4-triazol-1-yl)-1,3-butanediol.

This assessment was based on the followings:

1. The analytical method for Bayleton (none is available for Baytan, please see our discussion under Analytical Method in this petition), determines Baytan and its butanediol metabolite (KWG-1342), each with a separate peak and different retention time.

2. The available metabolism studies for Bayleton (none is available for Baytan), demonstrate that KWG 1323 is a direct metabolite of Bayleton (hydroxy Bayleton) with no demonstrated relationship between this metabolite and Baytan. On the other hand, KWG-1342 is a direct metabolite of Baytan (hydroxy Baytan). Therefore, until this is shown otherwise, KWG-1323 should not be included in the tolerance expression for Baytan.

3. In this petition, when Baytan was used on bananas, the bulk of the residues were in the form of KWG-1342 with little or no parent compound, Baytan, or, as expected, KWG-1323 metabolite.

There are no established tolerances for Baytan.

The chemical compound, Baytan, is a major metabolite of the fungicide, Bayleton, 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazole-1-yl)-2-butanone, and is included in the tolerance expression for Bayleton regulated as the combined residues of Bayleton and its metabolites containing chlorophenoxy and triazole moieties (expressed as the fungicide) (40CFR§180.410, 21CFR§193.83, and 21CFR§561.93). Tolerances are pending for Baytan and metabolites containing the chlorophenoxy and triazole moieties (sic) as follows:

PP#3F2854, A. Smith, 1/4/84- Tolerances resulting from the use of Baytan 150 FS, an aqueous mixture containing 13.8% active ingredient, equals to 1.25 lb ai/gal, as seed treatment of cereal grains: Grains of wheat, barley, oats, and rye (0.05 ppm); green forage of wheat, barely, oats, and rye (2.5 ppm; straws of wheat, barley, oats, and rye (0.1 ppm); corn fresh (including sweet) (K + cWHR), corn grain (including field and popcorn), and corn forage and fodder (0.05 ppm); meat, fat, and meat byproducts of cattle, goats, horses, and sheep (0.1 ppm); and milk, eggs, and meat, fat, and meat byproducts of poultry (0.01 ppm).

PP#5F3224/FAP#5H5458, M. Firestone, 5/31/85- Tolerances resulting from the use of Baytan 25% DF (BAY KWG 0519), as a foliar application by air or ground to wheat and grapes: Wheat grain (0.75 ppm); wheat green forage (85 ppm); wheat straw (17 ppm); grapes (0.5 ppm); meat, fat, and meat byproducts of cattle, goats, horses, and sheep (2.5 ppm); meat, fat, and meat byproducts of poultry (0.01 ppm); milk (0.1 ppm; and eggs (0.01 ppm). Food Additive Tolerances for grape juice (0.6 ppm) and wheat milled fractions, except flour (3.5 ppm). Feed Additive Tolerance for raisin waste (1.8 ppm).

Subsequent to the petition 5F3224 review, a Federal Register Notice [51FR(117)22124, 6/18/86] was published announcing that 40CFR§180 (subsection was not indicated) was amended by increasing the tolerance levels as follows: grapes 0.5 to 1.0 ppm; wheat grain 0.75 to 1.0 ppm; wheat green forage 85 to 100 ppm; and wheat straw 17 to 20 ppm. The same Notice announced amending 21CFR§193 and 561 (subsections were not indicated) by increasing the tolerance levels as follows: grape juice 0.6 to 1.5 ppm; wheat milled fractions, except flour 3.5 to 4.0 ppm; grape pomace 2.5 to 50 ppm; and raisin waste 1.8 to 5 pm.

Tolerances of 1.0 ppm on grapes and 1.0 ppm on wheat grain are established for Bayleton under 40CFR§180.410(a); and 4.0 ppm on wheat milled fractions, except flour, is established for Bayleton under 21CFR§193.83.

Tolerances regulated under Bayleton for wheat, green forage, and wheat straw are 15 and 5 ppm, respectively; and that for grape pomace and raisin waste are 3 and 7 ppm, respectively.

PP#4F3155, E. Haebrer, 2/6/85- Tolerances resulting from the use of Baytan 150 FS, an aqueous mixture containing 13.8% active ingredient (1.25 lb ai/gal) as seed treatment of grain sorghum: Sorghum grain (0.05 ppm); sorghum, green or dry forage (0.01 ppm).

Since Baytan is a metabolite of Bayleton, the tolerances for Bayleton and Baytan share common residues of concern. Therefore, 40CFR§180.3(d) applies. Accordingly, if and when

tolerances are established for Baytan, 40CFR§180.3(d) will need to be revised by addition of a subsection as follows: "Where tolerances are established for residues of both 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone and [beta-(4-chlorophenoxy)-alpha-(1,1-dimethyl-ethyl)-1H-1,2,4-triazole-1-ethanol], in or on the same raw agricultural commodity and its products thereof, the total residues of beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol; and its butanediol metabolite, 4-(4-chlorophenoxy)-2,2-dimethyl-4-(1H-1,2,4-triazol-1-yl)-1,3-butanediol shall not be higher than the beta-(4-chlorophenoxy)-alpha-(1,1-dimethyl- ethyl)-1H-1,2,4-triazole-1-ethanol tolerance".

Conclusions

1(a). For the purpose of the proposed use on bananas that will be imported to the United States, DEB concludes that the residues of concern for Baytan in bananas consist of the parent compound, Baytan, and its butanediol metabolite, KWG-1342.

1(b). There are no livestock feed items involved in the proposed use on bananas.

2. We conclude that adequate analytical methods are available for residue determination of Baytan and its butanediol metabolite in/on bananas. The method referred to in this petition has been recommended by the EPA for inclusion in PAM II as Bayleton Method III. The method may be used for enforcement of the proposed tolerance for residues of Baytan and its butanediol metabolite, KWG-1342, in/on bananas that will be imported into the United States. A copy of the proposed enforcement method is attached for convenience.

3. The petitioner is advised to revise Section F by indicating the chemical name of the parent compound and any metabolites of toxicological concern that ought to be regulated in the tolerance expression for Baytan. It is our assessment that tolerances for Baytan should be expressed as follows: "The combined residues of the fungicide, beta-(4-chlorophenoxy)-alpha-(1,1-dimethyl-ethyl)-1H-1,2,4-triazole-1-ethanol; and its butanediol metabolite, 4-(4-chlorophenoxy)-2,2-dimethyl-4-(1H-1,2,4-triazol-1-yl)-1,3-butanediol, calculated as beta-(4-chlorophenoxy)-alpha-(1,1-dimethyl- ethyl)-1H-1,2,4-triazole-1-ethanol.

4(a). The petitioner should explain what is meant by a production unit in terms of ai/acre.

4(b). The petitioner is advised to revise Section B by giving more details of the proposed use such as implement for applying the pesticide, depth of placing the pesticide in soil, method of applying the pesticide (foliar, broadcast, in furrow, rows, etc), and the PHI in days.

5. The petitioner should indicate the country or countries in which Baytan 3%G will be used and if the product is registered in those countries. If the product is not registered in those countries, the petitioner should tell us whether they intend to register it.

6. The raw agricultural commodity is the whole banana (pulp plus peel). Therefore, the petitioner should report on the total Baytan residues in/on whole banana or provide the weighs of banana pulp and peel for each residue value, as well as calculated values for the total residues in the fruit.

7. It appears from the data presented that the proposed 0.2 ppm tolerance for residues of Baytan in/on whole banana (of which no more than 0. 1 ppm for banana pulp) would be adequate. A final assessment on the tolerance, however, awaits the petitioner's response to the deficiencies cited under Recommendations .

8. We defer to the Registration Division for clearance of the inert ingredients in Baytan 3%G, proposed for use on bananas that will be imported into the United States.

9. An International Residue Limit Sheet is appended to this review (Attachment 2). There are no Codex, Mexican, or Canadian tolerances/limits currently established for Baytan (triadimenol, per se) on any crop. Thus, there are no compatibility problems at this time. Codex MRL's are currently established/proposed for the chemical, triadimefon, which includes triadimenol.

Recommendations

We recommend against the proposed tolerance of 0.2 ppm for residues of triadimenol and its butanediol metabolite in/on imported bananas because of Conclusions 3,4(a), 4(b), 5 and 6.

Notes to PM

1. If and when tolerances are established for Baytan, 40CFR§180.3(d) will need to be revised by addition of a subsection as follows: "Where tolerances are established for residues of both 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone and beta-(4-chlorophenoxy)-alpha-(1,1-dimethyl- ethyl)-1H-

1,2,4-triazole-1-ethanol, in or on the same raw agricultural commodity and its products thereof, the total residues of beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol, and its butanediol metabolite, 4-(4-chlorophenoxy)-2,2-dimethyl-4-(1H-1,2,4-triazol-1-yl)-1,3-butanediol shall not be higher than the beta-(4-chlorophenoxy)-alpha-(1,1-dimethyl- ethyl)-1H-1,2,4-triazole-1-ethanol tolerance.

2. If and when the requested tolerance for imported bananas is established, and TOX considerations permitting, it should be regulated under separate subsection in 40CFR§180.--- for "Tolerances with regional registration."

Detailed Considerations

Manufacturing and Formulation

The manufacturing process for Baytan and composition of the technical product are discussed in DEB's review of PP#3F2854, memo of A. Smith, 8/1/83. Based on an analysis of five batches, technical Baytan was found to range in purity from 92.7 to 90.0%. The impurities in technical Baytan are not likely to present a residue problem.

The formulation proposed for use on bananas is Baytan 3%G containing 3% triadimenol, the active ingredient in Baytan 25WP, which is the same as Summit 25%DF. The confidential statements of formula for Summit 25%DF and Baytan 3%G, are enclosed under section A in this petition. Clearance of the inert ingredients in the formulation is the purview of the Registration Division.

We defer to the Registration Division for clearance of the inert ingredients in Baytan 3%G, proposed for use on bananas that will be imported into the United States.

Proposed Use

For control of Sigatoka disease on bananas, the proposed use calls for one soil application of Baytan 3%G at the rate of 0.75 g ai/mat or 0.75 g act/pu (production unit). There is a 0-day PHI indicated in Section F, not in section B. The petitioner should explain what is meant by a production punch in terms of acre value.
The petitioner is advised to tell us the country or countries in which Baytan 3%G will be used and if the product is registered in those countries. If the product is not

registered in those countries, the petitioner should indicate whether he intends to register it. Furthermore, Section B should be revised to provide more details of the proposed use such as implement for applying the pesticide, depth of placing the pesticide in soil, method of applying the pesticide (foliar, broadcast, in furrow, rows, etc), and the PHI in days.

Nature of Residues

Plants

No plant metabolism studies are available for Baytan. Radiolabelled metabolism studies for Bayleton, a precursor of Baytan, have been reviewed in conjunction with PP#'s 2F2665, 2F2668, 2F2704, and 3F2887. In plants (apples, cucumbers, grapes, tomatoes, and wheat), Bayleton, 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone, is absorbed, translocated, and metabolized.

Metabolism studies have shown that the compound is rapidly converted to the reduction product, 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanol, also called KWG 0519, referred to as Baytan. Further metabolism can also occur in some crops, with hydroxylation occurring on the t-butyl group of the molecule to form the metabolite designated KWG 1342. To a lesser degree, Bayleton but not Baytan, can be metabolized to KWG 1323. Once hydroxyl groups are formed on these molecules, the potential for conjugation to naturally occurring plant materials is present. The structural formulas for these compounds are shown in Attachment 1 (one page).

For the purpose of the proposed use on bananas that will be imported to the United States, DEB concludes that the residues of concern for Baytan in bananas consist of the parent compound, Baytan, and its butanediol metabolite, KWG-1342.

Animals

No animal metabolism studies are available for Baytan. Radiolabelled metabolism studies for Bayleton, a precursor of Baytan, have been reviewed by DEB.

In animals (rats, cows, pigs, hens), Bayleton is metabolized and excreted with some transfer of residues to eggs and milk and deposition in tissues (PP#3F2887, memo of A. Smith, 9/12/83).

There are no livestock feed items involved in the proposed use on bananas.

Analytical Methodology

There are no methods for Baytan, per se, in plants or animals. The method used to quantitate residues of Baytan and its metabolites KWG 1342 and KWG 1323 in/on bananas is entitled "Residue Analysis Procedure for Bayleton and Metabolites in Barley and Wheat" (Mobay Report #80488, dated July 27, 1983). A discussion of this procedure can be found in DEB's review of PP#3F2887, memo of A. Smith, 9/12/83. The method has been judged adequate for enforcement of the existing tolerances for several plant and animal commodities. The method was recommended for inclusion in PAM II as Method III. The method determines bound and free residues of Bayleton, Baytan (KWG-0519), KWG-1342, and KWG-1323 as separate peaks with different retention times.

Briefly, the method involves sample extraction with methanol/water, cellulose hydrolysis to release bound residues, Gel permeation chromatography, and Florisil chromatography clean up. Baytan residues can be determined directly by GLC while sample fractions containing KWG-1342 and KWG-1323 are further derivatized with trifluoroacetic anhydride prior to quantitation of each fraction via GC.

Recoveries from banana pulp and peel that was fortified at 0.01 to 0.1 ppm with each of Baytan, KWG-1342, and KWG-1323 was reported at a minimum of 91% in the pulp and 77% in the peel for baytan and metabolites. Control pulp samples contained Baytan, KWG-1342 and KWG-1323 at a maximum level of 0.01, 0.02, and <0.01 ppm, respectively. Those in the peel were reported at 0.02, 0.03, and <0.01, in the same order.

Sample chromatograms are included.

The highest control value was considered to be the minimum detection level. Minimum detection level for Baytan and its butanediol metabolite, KWG 1342, were reported at 0.01 and 0.02, respectively, for a combined total of 0.03 ppm.
We conclude that adequate analytical methods are available for residue determination of Baytan and its butanediol metabolite in/on bananas. The method referred to in this petition has been recommended by the EPA for inclusion in PAM II as Bayleton Method III. The method may be used for enforcement of the proposed tolerance for residues of Baytan and its butanediol metabolite, KWG-1342, in/on bananas that will be imported into the United States.

Storage Stability For Baytan on Bananas

No storage stability studies are available for Baytan. A storage stability study for Bayleton was previously submitted and discussed in connection with PP#2F2665/FAP#2H5343 (memo of

A. Smith, 9/9/82). Data on the stability of Bayleton residues in plants under frozen conditions (-20°C) showed no significant decomposition of residues for samples that were held in storage for up to 299 days (forage) and 434 days (grains).

Residue Data For Baytan on Bananas

Data submitted reflect 11 field trials from Costa Rica and Honduras in which soil application of banana groves were made once to three times using 0.75 to 2.0 gm ai/pu (production unit) of Baytan 1% and 3%G. Banana samples were taken and frozen for a maximum of 180 days prior to analysis. The following is a summary of the test results:

gm ai per pu	No. of trt.	PHI in Days	Residues in ppm in/on Pulp Baytan	Pulp KWG1342	Pulp Total	Peel Baytan	Peel KWG1342	Peel Total
			Test # HON-BTEXT-86					
1	1	203	0.02	ND[1/]	0.04	0.30	0.05	0.35
		203	0.01	ND	0.03	0.14	0.08	0.22
			Test # COS-BTEXT-87H					
1.0	1	35	ND	ND	0.03	0.02	0.03	0.05
		49	ND	ND	0.03	0.01	<0.03	0.04
		63	ND	ND	0.03	0.01	<0.03	0.04
		79	ND	ND	0.03	0.02	<0.03	0.05
		91	0.02	ND	0.04	0.01	0.03	0.04
			Test #COS-BT005-87D					
1.0	1	12	ND	ND	0.03	0.03	<0.03	0.06
1.0	1	203	0.02	ND	0.04	0.3	0.05	0.08
0.75	1	261	0.02	0.02	0.04	0.02	0.04	0.06
	2	80	0.02	0.03	0.05	0.03	<0.03	0.06
	3	19	0.01	ND	0.03	0.02	0.04	0.06
2.0	1	7	0.10	ND	0.03	0.03	0.04	0.07
		35	ND	ND	0.03	0.01	<0.03	0.04
		49	ND	ND	0.03	0.01	0.04	0.05
		63	ND	ND	0.03	0.05	0.04	0.09
		79	0.01	ND	0.03	0.01	<0.03	0.04
		91	0.02	0.02	0.04	0.03	0.03	0.06
1.0	1	0	ND	ND	0.03	ND	ND	0.03
		14	ND	ND	0.03	ND	ND	0.03
		28	ND	0.02	0.03	ND	ND	0.03
		43	0.06	0.03	0.09	ND	0.70	0.08

gm ai per pu	No. of trt.	PHI in Days	Residues in ppm in/on Pulp Baytan	Pulp KWG1342	Pulp Total	Peel Baytan	Peel KWG1342	Peel Total
		61	ND	0.07	0.08	ND	0.14	0.15
		92	0.03	ND	0.05	0.03	ND	0.05
0.75	1	0	0.01	0.03	0.04	0.03	0.05	0.08
		14	ND	ND	0.03	0.01	0.02	0.03
		28	ND	ND	0.03	ND	ND	0.03
		43	ND	0.02	0.03	ND	ND	0.03
		61	ND	ND	0.03	ND	0.08	0.09
		92	0.02	ND	0.03	0.03	ND	0.05
0.75	3	130	0.04	ND	0.06	0.16	0.05	0.21
1.5	3	130	0.03	ND	0.05	0.3	0.12	0.42

1/ ND = Non-detectable (<0.01 ppm for Baytan and <0.02 ppm for KWG-1342)

Total Baytan and its butanediol metabolite, KWG-1342, in or on the whole banana fruit was not reported. The petitioner should report on the total Baytan residues in/on whole banana or provide the weighs of banana pulp and peel for each residue value for calculating the total residues in the fruit.

Calculated maximum residues in whole fruit was reported by the petitioner at 0.15 ppm (page 10), based on a 2:1 ratio of pulp to peel and using test results of HON-BTEXT-86 (0.04 ppm X 2/3 + 0.35 X 1/3). This test reflects one application using 1 gm ai/pu (1.34X), where samples were taken 203 days after application.

From the data presented, it is apparent that Baytan is taken up by the plant from the soil medium immediately after application, and translocated and metabolized. Measurable residues of Baytan and its butanediol metabolite were reported in the pulp and peel on day of application and at all reported PHI's ranging up to 203 days. The bulk of the residues, however, concentrate in the peel, almost 2 to 8 times that in the pulp, depending upon the dosage and/or number of applications. As it can be seen from the data presented, Baytan is showing some degree of persistence.

At the proposed use pattern, residues in the pulp and peel seems to have plateaued at about 2 months after application and began to decline approximately 3 months after application. Also, at the proposed rate, the amount of residues in the peel increases with increased number of applications. Residues in the pulp, although persistent, remain under 0.1 ppm at all dosages and PHI's tested (up to 2.7X rate and 203 day PHI).

It appears from the data presented that the proposed 0.2 ppm tolerance for residues of Baytan in/on whole banana (of which no more than 0. 1 ppm for banana pulp) would be adequate. A final assessment on the tolerance, however, awaits the petitioner's response to our request for total Baytan residues in/on whole banana including its butanediol metabolite, and an explanation of what a production unit means in terms of ai/acre.

Meat, Milk, Poultry and eggs:

There are no livestock feed items involved in the proposed use on bananas.

Other Considerations

An International Residue Limit Sheet is appended to this review (Attachment 2). There are no Codex, Mexican, or Canadian tolerances/limits currently established for Baytan (triadimenol, per se) on any crop. Thus, there are no compatibility problems at this time. Codex MRL's are currently established/proposed for the chemical, triadimefon, which includes triadimenol.

Attachments:

1. Metabolism in wheat (one page).
2. Codex Sheet (one page).
3. Analytical Method, entitled "Residue Analysis Procedure for Bayleton and Metabolites in Barley and Wheat", Mobay Report #80488, dated July 27, 1983, 24 pages.

cc With Attachments: S. Malak, **PP#8E3642**, and E. Eldredge (ISB/PMSD),
cc Without Attachment #3: PP#3F2854, PP#5F3224, PP#4F3155, Circulation, and RF.

RDI: P. V. Errico: 1/4/88: R. D. Schmitt: 1/4/88
TS-769C:DEB:HED:CM#2:Rm814A:S.Malak:X557-4379:s.m.:7/26/88, revised 12/8/88.