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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

JUN 20 1984

MEMORANDUM

SUBJECT: PP#4F3026: Tilt on bananas. Evaluation of analytical methods and residue data. Accession numbers: 072283, 072284, 072285.

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and

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Ciba-Geigy proposes a tolerance for residues of the fungicide CGA-64250 (Tilt, 1-(2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl)methyl-1H-1,2,4-triazole) and its metabolites determined as 2,4-dichlorobenzoic acid on bananas at 0.1 ppm.

No permanent tolerances are established for CGA-64250. A temporary tolerance on pecans has been approved by RCB (PP#1G2530, see memo of 2/10/84, L. Propst) and a permanent tolerance on pecans was proposed with PP#4F3007 (see memo of 5/15/84, A. Smith).

Conclusions

1. The nature of the residue in plants is adequately understood. The residue in plants consists of parent plus free and conjugated metabolites of parent that have been hydroxylated on the alkyl side chain of the dioxolane ring, free and conjugated components containing both the phenyl and triazole rings (CGA-91304, CGA-91305, and CGA-104284), and 1,2,4-triazole-1-alanine. With PP#4F3007 we deferred to TOX as to whether metabolites containing the triazole ring, but that would not be determined by methods that convert metabolites to 2,4-dichlorobenzoic acid, should be included in the tolerance expression for plants. We reiterate this deferral here.

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2. The nature of the residue in animals is adequately understood and is discussed in our review of PP#4F3007 (memo of 5/15/84, A. Smith); since no feed items are involved here, animal metabolism will not be further discussed.
3. The requirements for enforcement methodology await TOX's decision as to whether all major residues containing the triazole ring should be included in the tolerance. If these are included, then appropriate methodology will be needed. The petitioners have submitted a method that converts parent and metabolites to the triazole, but this method suffers from high blank values and poor recovery; it would not be suitable for enforcement unless it were modified. A second method (AG-356) converts residues to 2,4-dichlorobenzoic acid, and would be suitable for enforcement if triazole is determined to not be of concern and a method trial is successful. In any event, a method will be needed that determines the residue of concern at the tolerance level.
4. Since it is not known whether all major triazole containing metabolites will be included in the tolerance expression, we can make no conclusion as to an appropriate tolerance. If the residue of concern is limited to those metabolites determined by method AG-356, which converts residues to 2,4-dichlorobenzoic acid, then the submitted data would support a tolerance of 0.2 ppm; the proposed tolerance is 0.1 ppm. If all triazole containing metabolites are to be included in the tolerance expression, then additional residue data, as well as analytical methodology, will be needed.
5. Since no feed items are involved with the proposed use, there will be no problems of secondary residues in meat, milk, poultry, and eggs.
6. An International Residue Limits Status Sheet is attached. There is no Codex proposal step 6 or above, and Canada and Mexico have not established any Tilt residue limits on bananas. There will be compatibility problems.

Recommendation

We recommend against the proposed tolerance. Further consideration awaits TOX's answer to our deferral as to whether all triazole containing metabolites should be included in the tolerance expression. If these compounds are not to be included in the tolerance expression, then the submitted data would support a tolerance of 0.2 ppm on bananas, provided a method trial is successful. If triazole containing metabolites are to be included in the tolerance expression, then additional residue data and appropriate methodology will be needed. (Some triazole containing metabolites are indirectly determined by the method that converts metabolites to 2,4-dichlorobenzoic acid; other triazole containing

metabolites are not; it is these that we have expressed our concern to TOX about.)

DETAILED CONSIDERATIONS

Manufacture and Formulation

The manufacture of the technical material is discussed in our review of PP#1G2530 (memo of J. Worthington, 1/7/82). We expect no residue problems from the impurities.

The formulation proposed for use on bananas is Tilt 250 EC, an emulsifiable concentrate that contains 28.7% of the technical material (250g/L). The inert ingredients are cleared under 40 CFR 180.1001.

Proposed use

For control of yellow sigatoka, black leaf streak, black sigatoka, and leaf speckle disease (all caused by *Mycosphaerella* spp.), Tilt 250EC is to be applied at the rate of 0.4 L (100 g a.i.) per hectare at intervals of 14 to 28 days. Up to nine applications per season are allowed; there is no PHI.

Nature of the Residue

Plant metabolism studies have been carried out on peanuts, wheat, grapes, lettuce, carrots, and corn. Regardless of the plant to which it is applied CGA 64250 shows a similar metabolic pathway. These plants absorb, translocate, and metabolize CGA 64250; the major components of the residue consist of parent, four beta hydroxy isomers (hydroxylated on the alkyl group of the dioxolane ring), conjugates of these compounds, the ketone that results from hydrolysis of the dioxolane ring, the alcohol that results from reduction of this ketone, the olefin that results from eliminating water from the alcohol, and 1,2,4-triazole-1-alanine. Residues are determined by a combination of three methods, though no single available method will determine all components. With PP#4F3007 we deferred to TOX as to whether all major residues containing the triazole moiety should be included in the tolerance expression. We reiterate this deferral here.

Animal metabolism studies have been carried out on rats and goats and are discussed in our review of PP#4F3007 (see memo of 5/15/84, A. Smith). Since no feed items are involved with this petition, animal metabolism questions are not pertinent.

Analytical Methods

Three methods were used for collection of the residue data submitted with this petition. One method (AG-356) first converts residues to 2,4-dichlorobenzoic acid, which is then determined by GC/MS. The second method (REM-11/81) determines parent compound only, and the third method (AG-357) determines components containing

the triazole ring as the dibromo derivative.

AG-356

Residues are converted to 2,4-dichlorobenzoic acid by refluxing overnight with nitric acid. After dilution with water, the residues are partitioned into dichloromethane. Diazomethane is used to make the methyl ester, which is cleaned up by column chromatography on silica gel. Quantitation is by GC/MS. This method did not detect any residues (<0.04 ppm) in control bananas (peel or pulp). Reported recoveries are 83-137% (average = 104%) for pulp, 61-120% (103%) for peel, and 70-130% (94%) for whole fruit; all fortifications were at either 0.1 or 1 ppm.

REM 11/81

Samples are homogenized and extracted with methanol or aqueous methanol. The slurries are filtered and the residue in the filtrate is partitioned into dichloromethane. The dichloromethane is evaporated and the remaining residue is further cleaned up by column chromatography (alumina). Quantitation is by GLC with a flame ionization detector. Control samples of banana peels and pulp were consistently <0.02 ppm. Recoveries, at fortifications of 0.04 or 0.4 ppm, were 76-137% (average = 104%) for banana peels and 63-117% (89%) for pulp. Since no metabolites are determined, this method would not be suitable for enforcement or generation of residue data.

AG-357

A ground sample is refluxed with a solution of concentrated ammonium hydroxide/methanol, cooled, and then filtered. An aliquot is concentrated, then refluxed with a mixture of sulfuric acid, nitric acid, and water. The mixture is cooled and washed with dichloromethane. Sodium bromide and sodium bromate are used to make the 3,5-dibromo-1,2,4-triazole. The derivative is extracted into ethyl acetate, which is evaporated to dryness. The residue is taken up into hexane/toluene, then cleaned up on a silica gel column. Recoveries from fortified samples were low, about 60% for peel and 50% for pulp, and control samples were found to carry apparent residues of 0.2 ppm in pulp and 0.1 ppm in peel. The problems of poor recoveries and high control values preclude the possibility of this method being suitable for enforcement unless it was modified. We have made this conclusion earlier, with PP#4F3007 (memo of 5/15/84, A. Smith)

No conclusion as to appropriate methodology can be made until TOX responds to our deferral concerning triazole-containing metabolites. If triazole containing metabolites are to be included, then appropriate methodology will be needed. In any event, a method will be needed that determines the residue of concern at the tolerance level.

Residue data

Storage stability studies have been carried out on fortified soybeans and on peanut fodder, shells, and nutmeat carrying weathered residues. Loss of residue (as determined by method AG-356) on frozen storage over periods of up to 25 months is negligible. For the present petition banana samples were stored frozen for periods of up to 12 months.

Residue experiments were carried out in the Ivory Coast, Honduras, Martinique, and Belize. Residue data resulting from experiments that approximate the proposed use are summarized in the following table. A few residue data reflecting a 9 day PHI are included because of the high values. The proposed use allows up to nine applications of 100 g/ha; there is no PHI.

Country	Rate (g/ha)	no. appl.	PHI (days)	Total residue (ppm)	
				Pulp	Peel
Honduras†	100	6	0	0.042	<0.042
Honduras†	100	6	0	0.027	<0.042
Honduras†	100	6	0	0.023	<0.042
Martinique	100	1	0	<0.04	<0.042
Belize	100	1	1		<0.04*
Belize	100	9	0		<0.04*
Honduras	200	7	0	0.052	0.13
Honduras	200	7	0	<0.042	<0.042
Honduras	100	13	0	<0.042	0.043
Honduras	100	13	9	<0.02	0.19
Honduras	100	13	0	0.06	0.04
Honduras	100	13	9	0.18	0.12
Honduras	100	13	0	0.044	0.21
Honduras	100	13	9	0.042	0.10
Honduras	100	1	0	0.22**	0.13**
Honduras	100	1	0	0.18**	0.14**

†In these experiments, bananas were bagged before application.

*peel plus pulp

**These samples were determined by method AG-357, the triazole method; all other samples were determined by method AG-356, the 2,4-dichlorobenzoic acid method. All residues are expressed as CGA-65250 equivalents.

Samples from the Ivory Coast are not included above because these experiments incorporated PHI's of 5 days or greater; however, the data from the Ivory Coast are generally at the detection level and in no case higher than the above data. These data, along with residue data from other experiments involving multiple applications show that residues of CGA-64250 do not increase with time. Also not reported above are results from analyses using method REM 11/81, which determines parent compound only; these data are not considered useful for tolerance setting purposes.

Until TOX responds to our deferral concerning triazole, we can make no conclusion as to an appropriate tolerance level. If triazole containing metabolites are to be included in the tolerance expression, then additional residue data, as well as appropriate

methodology, will be needed.

If the residue of concern is limited to parent and metabolites containing the 2,4-dichlorophenyl moiety, then the submitted data are sufficient to support a tolerance of 0.2 ppm. This level is needed because, in Honduras, 13 applications of the proposed rate, 100 g/ha, resulted in residues of up to 0.18 ppm in pulp at a PHI of 9 days; residues had been <0.1 ppm at 0 days. This experiment involved an exaggerated number of applications at intervals less than that allowed by the label (9-11 days; the label stipulates intervals of 14-28 days between application), but the residue found was nearly twice that of the proposed tolerance.

Meat, Milk, Poultry, and Eggs

Since no feed items are involved here, there will be no problem of secondary residues in meat, milk, poultry, and eggs.

Other considerations

An International Residue Limit Status sheet is attached. There is no Codex proposal step 6 or above and Mexico and Canada have not established any Tilt residue limits on bananas. There will be no compatibility problems.