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

SEP 20 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#8F3674 -- Propiconazole (Tilt®) in/on Corn and Pineapple. Ciba-Geigy Amendment Dated 5/28/93.

DP Barcode: D191918. CBTS # 11976.

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THROUGH: Debra F. Edwards, Ph.D., Chief
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The present submission is a response to our 5/6/93 memo.

Conclusions (pertaining to this memo only)

1. Ciba-Geigy has satisfactorily responded to our request for storage information for the goat metabolism study. Analogous information is required for the poultry study.

2. Our requirement for storage stability of propiconazole in corn processed products remains (Conclusion #4a of our 5/6/93 memo).

3. Corrected calculations of recoveries in example corn processed fractions have been submitted.

Recommendation

CBTS continues to recommend against the proposed tolerances for reasons give in Conclusions 1 and 2. We would not object to issuance of a tolerance with expiration date while the requested storage stability data (Conclusion 2) are being generated.

Detailed Considerations

Deficiencies listed in our 5/6/93 memo are listed with Ciba-Geigy's response and CBTS' comments.

CBTS Deficiency #1b (Conclusion #1b from our 5/6/93 memo)

> The nature of the residue in ruminants and poultry will be understood once details of sample handling and length of storage for animal commodities have been submitted (PP#1F3974, S. Willett, memo of 6/11/91). The residue to be regulated is, tentatively, parent propiconazole and its metabolites analyzed as 2,4-dichlorobenzoic acid.

Ciba-Geigy Response

The in-life phase of the goat metabolism study occurred between May 23, 1989 and June 2, 1989. Milk, urine and feces were stored frozen immediately after collection. Liver, kidney, muscle and fat were stored frozen immediately after sacrifices. Samples were shipped frozen and then stored at -20°C until analysis. Processed tissues and extracts were kept at -20°C between bench workups and analyses. This period, which included processing, homogenization, combustion, extraction, and chromatography, lasted from about three to ten months. Times from initial storage to final analysis varied from 183-348 days.

Metabolite stability during storage at -20°C was checked by monitoring goat #73, day-4 urine using radiochromatography during the course of the study. Representative chromatograms are found in [MRID No. 42564006] and indicate no major qualitative changes to the metabolic profile for a period of about 220 days. In the case of the tissues, the samples remained in the freezer untouched for approximately 2 months before any laboratory procedures were begun. Since no degradation was observed during the analytical phase, it would seem unlikely that any losses could occur during the preliminary freezer stage. [Analysis of urine commenced 19 days after initial storage.]

CBTS Comment

As indicated in S. Willett's 6/11/91 memo for PP#1F3974, analogous poultry metabolism storage information should be submitted.

Our latest guidance document for plant and livestock metabolism studies, 7/16/92, states that "the present Agency position is that storage stability data should not normally be required for samples analyzed within 4-6 months of collection....." However, the above studies were conducted prior to issuance of this document. Because the metabolism of propiconazole is relatively straigtforward, CBTS does not think stability of propiconazole and metabolites under frozen storage conditions is a problem.

This deficiency remains, pending submission of requested poultry metabolism data.

CBTS Deficiency #4a

There are no storage stability data for residues of propiconazole and its metabolites in/on corn processed products (or any processed products). Stability in representative processed commodities should be demonstrated for periods up to 30 months. We suggest flour and refined oil.

Ciba-Geigy Response

Ciba acknowledges that there are no storage stability data on corn processed commodities but requests that the requirement for additional storage stability data be waived for the following reasons:

1. Stability has been demonstrated on peanut fodder, shells, and nutmeat for 25 months. In a continuing study stability data have been generated on grass seed, hay and forage through 25 months. Both studies have demonstrated 100% recoverability of residues at all time intervals.

2. The EPA-approved enforcement method for total propiconazole residues containing the 2,4-dichlorobenzyl moiety has been shown to be greater than 78-83% in ^{14}C-treated soybeans and 108-122% in ^{14}C-treated corn. Recoveries of 2,4-dichlorobenzoic acid (DCBA) from spikes of four metabolites varied from 76-105%, indicating quantitative conversion. Hence, if some degradation occurred this would only lead to degradates more easily converted to DCBA or possibly to DCBA itself.

3. The freezer storage time for the samples analyzed in the original processing study was only a maximum of 11 months, as opposed to 29-32 months in the current study. No residues were detected in grain or in processed commodities at 1X or 2X application rates. In addition, samples from three of the field corn trials in the orginal petition were analyzed after only 5-6 months of storage with no residues detected in any of the grain samples.

4. The requested stability study is of academic interest only. The product is applied prior to silking (before ear formation), it does not translocate, and even 5X applications do not result in any detectable grain residues. The stability data would have to be generated using parent fortifications which really does not provide confirmation of the stability of incurred residues.

CBTS Comment

While Ciba's arguments may be plausible, they are not sufficient to justify waiving of the storage stability requirement. Stability in a number of RACS surely makes it more likely that residues will be stable in other RACS and processed commodities, but data from only two crops are not sufficient. Although it may

be true that likely degradation products will be converted to DCBA, other degradation pathways cannot be ruled out. One definite possiblity would be irreversible binding of parent or degradates to the matrix. Parent fortifications yield useful information even if the results are not as definitive as those from studies using incurred residues.

CBTS would not object to issuance of a tolerance with expiration date while these data are being generated.

Deficiency #4b

> Examples of calculations used to determine percent recoveries in corn processed fractions should be submitted. [On page 11 of our 5/6/93 memo, we gave an example of a submitted calculation we could not verify.]

Ciba-Geigy Response

The previous submission contained a typographical error. Injected volumes which appear consistently throughout the report as 68 μg should in many cases be 135 μg. Corrected calculations for the two examples listed in the CBTS memo -- for chromatograms No. 79 and 83 -- are given.

CBTS Comment

This deficiency is resolved.

cc: RF, Circu., PP#1F3974, Mike Flood, E. Haeberer.
H7509C:CBTS:Reviewer(MTF):CM#2:Rm804P:703-305-7990:typist(mtf):9/20/93.
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