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

APR 28 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#'s 4F3074, 4F3007, and 4E3026. Propiconazole (Tilt® or CGA-64250) on Crops and Livestock Commodities. Results of the Multiresidue Method Testing. MIRD No. 40100101. RCB No. 2108.

FROM: Sami Malak, Ph.D., Chemist
Tolerance Petition Section III
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

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

THRU: Charles L. Trichilo, Ph.D., Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

Note: This is an expedited review at the request of the Registration Division's Director, Mr. E. F. Tinsworth (Letter of 4/14/87).

Introduction and Background

In response to RCB memo of subject petitions (A. Smith, 11/9/86), Ciba-Geigy submitted the results of the multiresidue method testing for the fungicide propiconazole (Tilt® or CGA-64250) as required in 40CFR§180.125(b)(15). In our memo of 11/9/86, RCB requested that residues of Tilt and its metabolites including 1,2,4-triazole, in or on crop samples and meat, milk, and egg samples must be subjected to analysis by the multiresidue protocols.

The document title for the multiresidue protocol is "Pesticide Assessment Guidelines, Subdivision O. Addendum, Residue Chemistry Data Requirements For Analytical Methods in 40CFR§180.125 Multiresidue Protocols."

51FR34249, 9/26/86 advise submitters to test the parent compound and all metabolites covered in the tolerance using FDA Multiresidue Method Protocols I, II, III, and/or IV. Further, the Notice recommends that data should be obtained from representative commodities from those crops and/or animal products within the pesticide petition under review. If tolerances are being requested on many crops in a group of related crops, only one crop in the group need be tested. The data developed under these protocols wil be submitted as entries in appropriate tables in the Pesticide Analytical Manual, Volume I.

Permanent tolerances are currently pending for residues of propiconazole (Tilt® or CGA-64250), 1-[[2(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl,-1-H1,2,4-triazole, in/on grains of wheat, barley, rye, and rice at 0.1 ppm; straw of wheat, barley, and rye at 1.5 ppm; rice straw at 3 ppm; kidney and liver of cattle, hogs, horses, sheep, and poultry at 0.1 ppm (PP#4F3074); pecans at 0.1 ppm (PP#4F3007); and bananas at 0.2 ppm (PP#4E3026).

In this submission, the study title for the multiresidue testing is "Determination of the Characteristics of Tilt and Its Metabolites, Including 1,2,4-Triazole, When Subjected to Analysis by the United States Food and Drug Administration (FDA) Multiresidue Protocols, I, II, III, and IV (Residue Analytical Method)." The study is authored by W. D. Rhoads, dated 2/25/87. The tests, identified as Ciba-Geigy No. 1055, were conducted by the Colorado Analytical Research & Development Corporation.

Experimental Variables

1. Test Compounds: Propiconazole or CGA-64250; Alkanol CGA-91305; B-hydroxy CGA-118244; and CGA-71019 (1,2,4-triazole). Test compounds were dissolved in acetone. Each test compound was then subjected to analysis using the five columns on both ECD and NPD (see below). The structural formulas of the test compounds is attached in Figure 1.

2. Test Commodities: Rice grain, rice straw, pecans, eggs, beef liver, whole milk, and meat.

3. Test Protocols: All four protocols I (PAM I, Method 211.1, 212.1, 252), II (PAM I, Method 232.3), III (PAM I, Method 232.4), and IV (PAM I, Method 242.2) were tested. Procedures were followed as outlined in each methodology.

4. GC Parameters For Protocols I, II, and III:

(a) GC Columns- Five gas chromatographic columns were used to determine the gas chromatographic profile of the test compounds. These were: 5% OV-101 on Chromosorb WHP 80/100; 3% OV-225 on Supelcoport 80/100; 2% poly diethylene glycol succinate (DEGS) on Chromosorb WHP 80/100; 3% OV-17 on Chromosorb WHP 80/100; and Ultra-Bond 20SE 80/100

(b) GC detectors- Since the test compounds do not contain phosphorous or sulfur, electron capture (ECD) and nitrogen specific detectors (NPD) were used for the GC studies.

(c) GC Calibration- Chlorpyrifos; p,p'-DDT; and parathion were used in the GC calibration with an ECD, whereas chlorpyrifos, parathion and monocrotophos were used in the calibration of the GC with an NPD.

(d) Detector Sensitiviy- The attenuation of the GC was adjusted to yield >50% full scale deflection for 1.5 nanograms chlorpyrifos injected.

Results and Discussion

A. Protocols I, II, and III

1. GC Analytical Behavior of Test Compounds When Subjected to the Procedures in Protocols I, II, and III.

Table 1 outlines the data obtained from the ECD and Table 2 outlines the data obtained from the NPD. Sample chromatograms of the test compounds are included. It is apparent that all test compounds are amendable to the GC method of analysis. In most cases, however, the GC peaks were broad with some tailing. With the exception of the triazole moiety, the remaining teste compounds studied were detected by Protocols I, II, and III. The triazole moiety (CGA-71019) was barley detectable in Protocol II and, because of interference, detection/ quantitation in eggs using Protocol III was not possible.

Table 3 outlines the amount of the individual test compounds required to produce an approximate 50% full scale deflection for the 5% OV-101 ECD system and for the 2% DEGS NPD system used in the study. The GC parameters were adjusted to yield a >50% full scale deflection for 1.5 nanograms of chlorpyrifos.

2. GC Parameters and RRc Calculations

Since the test compounds were found to be amendable to GC analysis and due to the fact that some slight variations of retention times and RRc values were found for the standards used for the calibration of the GC, the 3% OV-101 GC were adjusted to yield an RRc of p,p'-DDT of exactly 3.09. Using these parameters exact RRc values of 5.59 for propiconazole, 1.15 for CGA-91305 and 11.25 for CGA-118244 were obtained. The 2% DEGS GC parameters were adjusted to yield an RRc of parathion of exactly 2.5. Using these parameters an exact RRc values of 0.31 for CGA-71019 was obtained. These data are outlined in Table 4. Sample chromatograms of this calibration study are included.

3. Recovery of Test Compounds

(a) Protocol I. Through Florisil Cleanup Column:

The folrisil used in this study was calibrated with lauric acid and further standardized using heptachlor epoxide and endrin. Using an external standard quantitation, 126.8% of the heptachlor epoxide was found in the diethyl ether/Petroleum ether (94/6) eluant and 112.6% of the endrin was found in the diethyl ether/petroleum ether (15/85).

Fifteen ml of the stock solution (100 micrograms/ml in acetone) were used for each test compound. Theoretical values for each analyte were calculated to be 3 micrograms/ml [(100 micrograms x 15 ml)/500]. Using external standard calibration the petroleum ether florisil column load solution was found to contain 1.73 micrograms/ml of propiconazole, 1.55 micrograms/ml of CGA-91305, 0.57 micrograms/ml of CGA-118244 and 3.0 micrograms/ml of CGA-71019. Table 5 outlines recovery data for the four test compounds taken through the two florisil elution studies. As can be seen from the data outlined in Table 5 none of the four test compounds eluted in excess of 10% from the florisil columns, with the six eluants studied. Representative chromatograms of these florisil studies and standardization data using 5% OV-101 EC system are included.

(b) Protocol II. (1) Through Cleanup Column:

Fifty micrograms of each test compound was added to the charcoal column and the cleanup followed as per

Procedure II. Using the 5% OV-101 EC/GC system CGA-91305 was recovered in the amount of 1.3-1.6%; propiconazole was recovered in the amounts of 53.1-66.1%; and CGA-118244 was recovered in the amounts of 12.4-10.6%. Using the 2% DEGS NPD system, CGA-71019 was recovered in the amounts of 0.2-0.4%. Representative chromatograms of these studies are included.

(2) Through Complete Method:

Since propiconazole was recovered from the charcoal column in excess of 30%, the complete method was undertaken as per Ciba-Geigy protocol 206-86. Pecan nutmeats (211.13K), dairy milk (211.13h), beef round (211.13a and f) and beef liver (211.13a and f) were subjected to PAM I 211 extraction methodology and the 232.34 charcoal column methodology.

Pecan nutmeats, dairy milk and meats were fortified with propiconazole at levels from 0.05 to 0.2 ppm. Table 6 outlines the recovery data. It can be seen that propiconazole is recovered from all solutions.

Recovery from pecan nutmeats was greater than 100%, from dairy milk renged from 23.6 to 47.1%, from beef round ranged from 12.6 to 47.1%, from beef liver ranged from 14.1 to 34.5%. Thes data demonstrate that propiconazole is amendable to analysis using PAM I 211 and 232.34 methodology. Adequate chromatograms from Protocol II are included.

(c) Protocol III. Through Complete Method:

Rice straw, rice grain and eggs were subjected to PAM I 232.43 acetone extraction and partition methodology. Rice straw was fortified at 0.05 to 6 ppm levels of the test compounds. Rice grain and eggs were fortified at 0.05 and 0.1 ppm levels of the test compounds. Table 7 outlines recovery data of the test compounds, as well as, control and reagent blank data.

As can be seen in Table 7, the reagent blank did not produce any interference peaks which would effect the analysis of propiconazole, CGA-91305 or CGA-118244. An interference peak equivalent to 0.012 ppm was found for CGA-71019. The analysis of control rice straw, rice grain and eggs for the four test compounds showed no interferences for propiconazole; however, rice straw yielded an 0.14 ppm background for CGA-91305; rice straw and rice grain yielded an 0.17 ppm background for

CGA-118244; and eggs was reported to contain sufficient volatile material to keep the recorder off scale for the CGA-71019 retention time range.

Recovery data for the three substrates studied demonstrate that all four test compounds are recovered from rice straw; rice grain; and that propiconazole, CGA-91305, and CGA-11844 are recovered from eggs. CGA-91305 was not recovered from rice grain. Interference did not allow quantitation of CGA-71019 in eggs.

Recovery data outlined in Table 7 demonstrate that the four test compounds are amendable to analysis using the PAM I 232.43 methodology. Typical chromatograms from Protocol III study are included.

B. Protocol IV

An HPLC was used in this study. Calibration was accomplished by the use of carbofuran, carbaryl, methiocarb and methomyl.

The four test compounds were dissolved in methanol and 10 nanograms of each subjected to the carbamate post column fluorescence labeling analysis. None of the four test substances were detected. The test substances were then chromatographed along with carbofuran, without the post column fluorescence labeling, to determine if naturally fluorescent properties were present. All four analytes, as well as, carbofuran generated flat baselines when subjected to HPLC analysis in which the post column system was by-passed. These data demonstrate that none of the four test compounds was detectable under Protocol IV. Adequate chromatograms are included.

Summary

Propiconazole and its metabolites; Alkanol CGA-91305; B-hydroxy CGA-118244; and CGA-71019 (1,2,4-triazole) were subjected to the Multiresidue method of analysis in PAM I, Protocols I (211.1, 212.1, 252), II (232.3); III (232.4), and IV (242.2). Test commodities included rice grain, rice straw, pecan nutmeats, eggs, beef liver, whole milk, and meats.

Protocol I: All four test compounds were amendable to GC analysis. In some cases, the GC peaks were broad and tailing. However, the four test compounds were detectable by Protocol I.

Protocol II: Of the four test compounds studied, only propiconazole was recovered in excess of 30% through the charcoal column.

Protocol III: With the exception of the triazole moiety the remaining test compounds were amendable to analysis from rice straw, rice grain, and eggs. Because of interference, detection/quantitation of the triazole moiety in eggs could not be achieved in this protocol.

Protocol IV: None of the four test compounds was detected under this Protocol.

Conclusions and Recommendations

Propiconazole (Tilt®) and three of its metabolites, including the triazole moiety, were subjected to the Multiresidue Method of Analysis of PAM I, Protocols I, II, III, and IV. None of the test substances was detectable by Protocol IV. With the exception of the triazole moiety, the remaining test compounds studied were detected by Protocols I, II, and III. The triazole moiety (CGA-71019) was barley detectable in Protocol II and, because of interference, detection/quantitation in eggs using Protocol III was not possible.

We recommend forwarding the data package to the FDA for their evaluation and inclusion of the recovery data for propiconazole in the appropriate Tables in PAM I, Multiresidue Test Results as required in 40CFR§180.125 (b)(15).

Attachments: Figure 1 and 7 Tables (8 pages, copied from Ciba-Geigy's submission).

cc: With Attachments: Circu, RF. SF (propiconazole or Tilt®), S. Malak, M. Bradley, FDA, PP#4F3007, PP#4F3074, PP#4E3026, and PM # 21.

RDI: P. V. Errico:4/24/87:R. D. Schmitt:4/24/87
TS-769C:RCB:CM#2:RM814A:S.Malak:X557-4379:4/23/87

TILT CGA-64250 Reviews

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The next 8 page(s) is/are not included in this copy of the TILT reviews.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commerical/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

_X_ Detailed methods and results of a registrant submission.

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