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

MAY 10 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F3337 - Metalaxyl on Strawberries - Evaluation
of Amendment Dated November 4, 1988 (MRID Nos. 408804-
00 and 408804-01) (DEB Nos. 4814, 4815, and 4816)

FROM: Martin F. Kovacs, Jr., Ph.D., Chemist
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TO: Susan Lewis, Acting PM 21
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and

Toxicology Branch II
Herbicide, Fungicide and Antimicrobial Support
Health Effects Division (H7509C)

THRU: Richard Schmitt, Ph.D., Acting Chief
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Richard D. Schmitt

Background

Ciba-Geigy Corporation has submitted this amendment consisting of a cover letter dated November 4, 1988, a revised Section B, a revised Section D (results of 15 additional residue trials on strawberries conducted in 10 different states), and a revised Section F (increasing the proposed tolerance for residues of metalaxyl on strawberries from 5 to 10 ppm) in response to Deficiency 3 cited in DEB's (M.P. Firestone) reviews of February 21 and September 8, 1986 of PP#6F3337.

DEB previously recommended in the M.F. Kovacs September 3, 1987 review of PP#6F3337 against the proposed 5.0 ppm tolerance with regional registration for the use of metalaxyl

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on annual strawberries grown in California only for the reasons cited under Criteria Nos. 2, 3, and 4 of EPA's Policy Statement on Minor Uses of Pesticides (FR Vol. 51, No. 63, April 2, 1986, pages 11341-11346).

Summary of Deficiencies Remaining to be Resolved

The apparent discrepancies between the newly proposed use pattern described in the current revised Section B/label (1 to 2 lb ai/A/application) and that indicated in the submitted strawberry residue trials (1 lb ai/A/application) need to be addressed and reconciled by the petitioner. Also, the "Note" on the proposed label limiting use to 2 lb ai/A/year needs to be clarified, since the use directions imply a permissible seasonal use rate of 3 to 6 lb ai/A. A revised Section B/label is needed. [The available data will support the proposed tolerance provided use is limited to a single fall application at transplanting at 1 to 2 lb ai/A, followed by two applications at 1 lb ai/A or one application at 2 lb ai/A during the growing season.]

Recommendations

DEB recommends against the establishment of the proposed 10 ppm tolerance for the reason given above. Requirements for resolution of this deficiency are also discussed in the appropriate conclusions under the "Present Considerations" section that follows in this review.

Conclusions

1. The petitioner has favorably responded to the intent of Deficiency 3 (Conclusion 3) of the M.P. Firestone February 21, 1986 review of PP#6F3337 by submitting strawberry residue trials reflecting 2-3 applications at 1 to 2 lb ai/A and minimum PHI (0 days) from the States of New York, North Carolina, Pennsylvania, Michigan, Ohio, Oregon, Washington, California, Florida, and Louisiana. Therefore, the original Deficiency 3 has been resolved. However, in the process of submitting the new strawberry residue studies, together with a newly revised Section B/label and a revised Section F, the petitioner has now generated additional concerns that require resolution (see Conclusions 2 and 3 discussed below).
2. The apparent discrepancies between the proposed use pattern described in the current revised Section B/label (1 to 2 lb ai/A/application) and that indicated in the currently submitted strawberry residue trials (1 lb ai/A/application) need to be

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addressed and reconciled by the petitioner. Also, the "Note" on the proposed label limiting use to 2 lb ai/A/year needs to be clarified, since the use directions imply a permissible seasonal use rate of 3 to 6 lb ai/A.

3. The available residue data will support the proposed tolerance, provided use is limited to a single fall application at transplanting at 1 to 2 lb ai/A, followed by two applications at 1 lb ai/A or one application at 2 lb ai/A during the growing season.

Present Considerations

The remaining deficiency cited in DEB's February 21, 1986 review is restated below followed by the petitioner's responses and DEB's comments.

Deficiency (Conclusion) 3

The residue data do not support the proposed metalaxyl use on strawberries for the following reasons:

- a. Three out of seven field studies (including both non-California studies) do not reflect the proposed 0-day PHI; California = 68 days, Maryland = 40 to 54 days, Louisiana = 21 to 35 days.
- b. No field trials were conducted in the Pacific Northwest (Oregon or Washington), the Northeast (New York, Pennsylvania, or New Jersey), the Midwest (Michigan or Ohio), or Florida, areas in which strawberry agricultural practices are expected to vary.

Thus, the petitioner will need to conduct additional field trials in the States of Oregon or Washington; New York, Pennsylvania, or New Jersey; Michigan or Ohio; and Florida, which reflect the maximum proposed use (3 applications at 1.0 lb ai/A) and minimum PHI (zero-days).

At this time, DEB can reach no conclusion regarding the adequacy of the proposed 5 ppm metalaxyl tolerance for strawberries.

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Petitioner's Response to Deficiency (Conclusion) 3

In addition to Ciba-Geigy's cover letter from Karen S. Stumpf (Senior Regulatory Specialist) to Lawrence J. Schnaubelt (EPA/RD PM 21) dated November 4, 1988 the following documents were submitted:

1. Revised Section B (MRID No. 408804-00), Supplemental Labeling dated November 4, 1988 for Ridomil® 2E Fungicide, EPA Registration No. 100-607, and a Revised Section F dated November 4, 1988 as follows:

REVISED
SECTION B

AMOUNT, FREQUENCY, AND TIME OF APPLICATION
OF METALAXYL TO STRAWBERRIES

Strawberries

Metalaxyl provides control of red stele (Phytophthora fragariae), vascular collapse (P. cactorum), and leather rot (P. cactorum) when used as directed. Applications may be made using ground application equipment or through irrigation systems.

Annual Strawberries (Vascular Collapse): Apply metalaxyl at 1-2 lb ai/treated acre in sufficient water to move the fungicide into the root zone of the plants. Make one application at the time of transplanting. Make an additional application 30 days before the start of harvest and another one in July before the second flush. For banded applications, a 12-inch band is recommended. Use the formula in the General Information section of this label to determine the amount of metalaxyl needed per acre. When metalaxyl is applied through drip irrigation systems, use the same amount as would be applied in a 12-inch band. Observe the precautions concerning application of metalaxyl through irrigation systems in the General Information section of this label.

Perennial Strawberries (Red Stele and Leather Rot): Apply metalaxyl at 1-2 lb ai/treated acre in sufficient water to move the fungicide into the root zone of the plants. Make one application at the time of transplanting or in the spring before the plants start growth. Make another application in the fall after harvest. For control of leather rot, an

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application can be made during the growing season. Use sufficient water to move metalaxyl into the root zone. For banded applications, a 12-inch band is recommended. Use the formula in the General Information section of this label to determine the amount of metalaxyl needed per acre.

Note: To avoid possible illegal residues, do not use more than a total of 2 lb of metalaxyl active ingredient per acre of strawberries per year.

REVISED
SECTION F

PROPOSED PESTICIDE TOLERANCES

We hereby request a tolerance for combined residues of the fungicide, metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester], and its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl) alanine methyl ester, each expressed as metalaxyl, in or on the raw agricultural commodity strawberries at 10.0 parts per million (ppm).

2. Ciba-Geigy Report No. ABR-88131 (MRID No. 408804-1) dated September 30, 1988; Response to EPA Review of Metalaxyl (Ridomil 2E) on Strawberries Including Results of Additional Field Trials

Analytical Methodology

No new analytical methodology for strawberries was submitted by the petitioner with this amendment.

The analytical methodology used to generate the strawberry residue data in the submitted 1987/1988 trials is titled "AG-395 Improved Method for the Determination of Total Residues of Metalaxyl in Crops as 2-6-Dimethylaniline," K. Balasubramanian, R. Perez dated December 12, 1982. [This method was subjected to a successful method trial in conjunction with PP Nos. 3F2918 and 3F2919 (see K. Arne memorandum of August 2, 1984).]

This total residue method is used for the determination of the combined residues of metalaxyl (N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, methyl ester) and its metabolites which contain the 2,6-dimethylaniline moiety: N-(2-hydroxymethyl)-6-methylphenyl)-N-(methoxyacetyl)alanine, methyl

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ester (CGA-94689); N-(2,6-dimethylphenyl)-N-(hydroxyacetyl) alanine (CGA-107955); N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine (CGA-62826); and N-(2,6-dimethylphenyl)-N-(hydroxyacetyl) alanine, methyl ester (CGA-67869).

In brief, strawberry samples are extracted by homogenization with 80 percent methanol/water and filtered through Whatman 2V filter paper. The extract is evaporated to dryness, a small amount of distilled water is added, then the extract is refluxed upon addition of methanesulfonic acid. Water is added followed by neutralization with sodium hydroxide (25%). The 2,6-dimethylaniline (2,6-DMA) formed under acid hydrolysis is steam distilled, and then cleaned up with a silica Sep Pak column. Quantitation of 2,6-DMA is performed by capillary gas chromatography using a NPD detector in the nitrogen specific mode.

At fortification levels of from 0.05 to 2.0 ppm metalaxyl, recoveries from strawberries ranged from 62 to 133 percent (average of 50 samples = 83%). Of 37 controls, 23 were reportedly < 0.05 with 14 ranging from 0.05 to 0.31 ppm. In any case, these values are well below the proposed 10 ppm metalaxyl tolerance for strawberries.

Residue Data

Strawberry samples analyzed in conjunction with this petition were stored under frozen conditions prior to analysis for periods of time ranging from 2 to 14 months. [Storage stability studies of metalaxyl in potatoes and tobacco, reviewed in conjunction with PP#1F2500 (see P. Errico memorandum of March 9, 1982), show that residues are stable at 5 °F for at least 18 months.]

Residue trials (7) were conducted on perennial strawberries during the 1986/1987 growing seasons in the States of New York, North Carolina, Pennsylvania, Michigan, Ohio, Oregon, and Washington. Residue trials (8) were conducted on annual strawberries during either the 1986/1987 or 1987/1988 growing seasons in the States of California (4), Florida (3), and Louisiana.

In all trials, Ridomil 2E was applied by either of two methods as follows:

1. A drench broadcast application of 1.0 lb ai/A in the fall, at transplanting to annual strawberries or to

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established plants of perennial strawberries, followed by two subsequent drench broadcast applications of 1.0 lb ai/A in the spring.

2. A drip irrigation application of 1.0 lb ai/A in the fall, at transplanting to annual strawberries, followed by two subsequent drip irrigation applications of 1.0 lb ai/A in the spring.

A 2X rate using Ridomil 2E at 2.0 lb ai/A/application was also applied for comparison purposes. Fruit samples from the drench broadcast applications were collected at 0 days after the second application before irrigation and at 0 days after the third application before and after irrigation. Additional samples from selective tests were taken at 7, 14, and 21 days after the third application to obtain residue decline data. Fruit samples from the drip irrigation applications were collected at 0, 7, 8, 14, 15, and 21 days after the second and third applications.

Using the drench broadcast application method and a use rate of 1.0 lb ai/A/application of Ridomil 2E with a 0-day PHI, residues of metalaxyl and its metabolites on perennial strawberries ranged from 0.36 to 1.90 ppm and averaged 0.96 ppm following two applications and ranged from 0.7 to 7.8 and averaged 2.7 ppm following three applications. The maximum reported residue value of 7.8 ppm was obtained following three applications in the New York trial.

Using the same method of treatment, treatment schedule, and PHI described above, residues of metalaxyl and its metabolites on annual strawberries ranged from 1.1 to 4.4 ppm and averaged 2.66 ppm following two applications and ranged from 0.83 to 5.1 ppm and averaged 2.23 ppm following three applications. The maximum reported residue value of 5.1 ppm was obtained following three applications in the Louisiana trial.

Using the drip irrigation method of application and a use rate of 1.0 lb ai/A/application of Ridomil 2E with a 0-day PHI, residues of metalaxyl and its metabolites on annual strawberries ranged from < 0.05 to 0.30 ppm and averaged 0.11 ppm following two applications and ranged from 0.08 to 1.30 ppm and averaged 0.52 ppm following three applications. Additional residue data reflecting two or three applications at 1.0 lb ai/A/application and PHIs ranging from 7 through 21 days were also reported for drip irrigation treatments. The maximum reported residue obtained from the latter data, 3.4

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ppm, reflected three applications at an 8-day PHI for a California trial. According to the petitioner, residues plateaued between 7 and 14 days following drip irrigation treatments.

Eighteen additional drench broadcast (14) and drip irrigation (4) trials at the higher application rate of 2 lb ai/A were conducted in New York (2), North Carolina (2), Michigan (2), Washington (2), California (6), and Florida (4). Both annual and perennial strawberries were represented in the drench broadcast trials, while drip irrigation trials included annual strawberries only. Combined residues of metalaxyl and its metabolites before irrigation on the day of the last of two drench broadcast application ranged from 2.0 to 8.3 ppm (average = 4.1 ppm). On the day of the last of three drench broadcast applications, residues ranged from 0.93 to 13 ppm (average = 4.3) before irrigation and 1.0 to 13 ppm (average = 4 ppm) after irrigation (all residues before and after irrigation were \leq 4.6 ppm, except in one New York trial). Two broadcast drench trials from California and Florida included analyses 7 to 8, 14, and 21 days after the last of three applications at 2 lb ai/A/application. Residues ranged from 0.53 to 2.7 ppm after 7 to 8 days, 1.2 to 2.2 after 14 days, and 0.3 to 1.3 after 21 days (all values reflect postirrigation residues). The drip irrigation residue trials also included analyses at 7 to 8, 14, 15, and 21 days after the final treatment. Residues were 0.22 to 2.9 ppm on the day of the last of two to three applications at 2 lb ai/A/application, 0.12 to 3.3 ppm after 7 to 8 days, 0.13 to 2.8 ppm after 14 to 15 days and 0.44 to 1.9 ppm after 21 days.

In all residue trials, results were corrected for average recovery values but not for control values.

DEB's Comments/Conclusions re: Deficiency (Conclusion) 3

1. Revised Section B

For perennial strawberries, the revised Section B/label indicates that metalaxyl applications at 1 to 2 lb ai/A are permitted in the spring, during the growing season, and in the fall after harvest for a total of 3 to 6 lb ai/treated acre per year. However, the "Note" which appears on the revised label restricts metalaxyl use to no more than a total of 2 lb ai/A of strawberries per year. Is it the

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petitioner's intent to impose the 2 lb ai/A use limitation during the growing season or when berries are present? If so, then a revised Section B/label must be submitted by the petitioner clarifying the maximum number of applications and lbs of ai/A permitted on both annual and perennial strawberries during the growing season or when berries are present.

The current Section B/label implies that applications up to 2 lb ai/A/application are permitted for both annual and perennial strawberries during the growing season whereas the residue data submitted in this amendment on both annual and perennial strawberries indicate that the 1X single application rate is 1 lb ai/A.

Deficiency I

The apparent discrepancies between the proposed use pattern (1 to 2 lb ai/A/application) described in the current Section B/label and that indicated in the submitted strawberry residue trials (1 lb ai/A/application) need to be addressed and reconciled by the petitioner in a new revised Section B/label. Also, the "Note" on the proposed label limiting use to ≤ 2 lb ai/A/year needs to be clarified, since the use directions imply a permissible seasonal use rate of 3 to 6 lb ai/A.

2. Residue Data/Revised Section F

Since the reported residues of metalaxyl and its metabolites on either annual or perennial strawberries did not exceed the proposed 10 ppm tolerance following 2 applications at the maximum proposed single application (2 lb ai/A) rate the proposed tolerance appears to be adequate. However, the petitioner must submit a revised Section B/label clarifying the intended use pattern on strawberries. The available data will support the proposed tolerance provided use is limited to a single fall application at transplanting at 1-2 lb ai/A, followed by two applications at 1 lb ai/A or one application at 2 lb ai/A during the growing season. Upon receipt of the revised Section B/label and its favorable evaluation by DEB, we will be able to recommend for establishment of the proposed 10 ppm tolerance.

The petitioner has favorably responded to the intent of Deficiency 3 (Conclusion 3) of the M.P. Firestone February 21, 1986 review of PP#6F3337 by submitting strawberry residue trials reflecting two to three

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applications at 1 to 2 lb ai/A and the minimum PHI (0 days) from the States of New York, North Carolina, Pennsylvania, Michigan, Ohio, Oregon, Washington, California, Florida, and Louisiana. Therefore, the original Deficiency 3 has been resolved. However, in the process of submitting the new strawberry residue studies, together with a newly revised Section B/label and a revised Section F, the petitioner has now generated additional concerns (deficiencies) that require resolution (see Deficiency I discussed previously).

Other Considerations

An International Residue Limit (IRL) Status sheet is included with this review as an attachment. Canada and Mexico have no established limit/tolerance covering residues of metalaxyl in/on strawberries. Also, the proposed U.S. tolerance for metalaxyl and its metabolites on strawberries cannot be harmonized with the Codex IRL on strawberries (0.2 ppm) because the Codex IRL covers only parent residues. [It would not be possible to estimate residues of the parent per se from U.S. residue trials because a "total residue" method that converts metalaxyl and its metabolites to a common moiety prior to analysis (2,6-dimethylaniline) was used in residue analysis.]

Attachment: International Residue Limit Status sheet

cc:R.F.,Circu.,Reviewer(M. Kovacs),PP#6F3337,PMSD/ISB (Eldredge)

RDI:D.F.Edwards:05/02/89:R.A.Loranger:05/2/89

H7509C:DEB:Rm812:x7689:Tvpist Kendrick: edited by mk:5/8/89

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL METALAXYL

CODEX NO. 136

F. J. ...
5/1/87

CODEX STATUS:

No Codex Proposal
Step 6 or above

PROPOSED U.S. TOLERANCES:

Petition No. 6F 3337

RCB Reviewer MARTIN F. KOLLER, JR

Residue (if Step 8): _____

metalaxyl per se

Residue: METALAXYL AND ITS METABOLITES
CONTAINING THE 2,6-DIMETHYLAMINO MOIETY, AND
(2-HYDROXYMETHYL-6-METHYL-PHENYL)-L-ALANINE
ACETYL ALANINE METHYL ESTER, WHICH IS EXPRESSED
AS METALAXYL

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
<u>strawberry</u>	<u>0.2</u>

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
<u>STRAWBERRIES</u>	<u>10.0</u>

CANADIAN LIMITS:

No Canadian limit (on strawberries)

Residue: _____

percent only

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
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MEXICAN LIMITS:

No Mexican limit

Residue: _____

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
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NOTES:

For negligible residue tolerances on plates