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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F3337 (RCB#360) - Metalaxyl on Strawberries -
Evaluation of Analytical Methods and Residue Data
(Accession Numbers 260658 and 260659)

FROM: Michael P. Firestone, Ph.D., Chemist
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and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

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

[Signature]

Ciba-Geigy Corporation is requesting establishment of 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 5.0 parts per million (ppm).

Metalaxyl tolerances are currently established on a wide variety of raw agricultural commodities (RAC's) at levels ranging from 0.02 to 10 ppm (see 40 CFR 180.408). Tolerances

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are pending on several crops, however, Residue Chemistry Branch (RCB) has recently recommended in favor of tolerances for residues of metalaxyl in asparagus at 7 ppm (see M. Firestone memorandum of February 7, 1986 re: PP#6F3330) and in raspberries at 0.5 ppm (see M. Nelson memorandum of July 6, 1983, re: PP#3F2848).

Conclusions

1. The nature of the residue in plants and animals is considered adequately understood for the purposes of supporting the proposed metalaxyl use on strawberries. The residues of concern consist of parent compound metalaxyl and its metabolites containing the 2,6-dimethylaniline moiety, and N-[(2-hydroxymethyl)-6-methylphenyl]-N-(methoxyacetyl)alanine, methyl ester.
2. Adequate analytical methodology is available to enforce the proposed tolerance for residues of metalaxyl in/on strawberries.
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-CA studies) do not reflect the proposed zero-day PHI; CA = 68 days, MD = 40 to 54 days, LA = 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, RCB can reach no conclusion regarding the adequacy of the proposed 5 ppm metalaxyl tolerance for strawberries.

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4. Since strawberries are not considered an animal feed item, there is little likelihood of secondary residues occurring in meat, milk, poultry, and eggs as a result of the proposed metalaxyl use on strawberries.
5. An International Residue Limit Status sheet is included with this review as Attachment 1. Since Codex, Canada, and Mexico have no established limit/tolerance covering residues of metalaxyl in/on strawberries, there is no compatibility problem.

Recommendation

At this time, RCB recommends against the proposed metalaxyl tolerance covering residues in/on strawberries for the reason cited under Conclusion 3 above.

Note to the Product Manager

RCB has considered whether the proposed use of metalaxyl on strawberries could qualify for a tolerance with regional registration based on EPA's Revised Draft Policy Statement on Minor Uses of Pesticides (OPP-30099 - see S. Schatzow memorandum of December 24, 1985), in lieu of the relevancy of the residue data generated only in California.

Although strawberries are not included in the list of minor crops automatically considered for a pesticide tolerance with regional registration, the Agency will consider other crops (such as strawberries) for tolerances based on geographically limited residue data on the basis of the following criteria:

1. Likelihood of expanded use,
2. Quality of the available residue data,
3. Availability of data on similar crops,
4. Variability of the residue data base, and
5. Toxicity of the pesticide.

On the basis of the above criteria for a tolerance with regional registration in the State of California only, RCB

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finds that it cannot translate raspberry residue data (the only berry crop for which a metalaxyl tolerance exists) since residues in/on strawberries are likely to be 10 times higher than those in/on raspberries. Also, metalaxyl is a systemic pesticide. Judgment on matters relative to Criteria No. 1 (Likelihood of expanded use) above should be referred to the Benefits and Use Division.

Thus, additional data as cited under Conclusion 3 above are required to support the proposed metalaxyl tolerance for strawberries.

A copy of EPA's Revised Draft Policy Statement on Minor Uses of Pesticides (OPP-30099) is attached to this review.

DETAILED CONSIDERATIONS

Manufacture and Formulation

The manufacturing process for metalaxyl is discussed in RCB's review of PP#1F2500 (see P. Errico memorandum of March 9, 1982). RCB has previously concluded that impurities in the technical chemical are not likely to present a residue problem (see G. Makhijani memorandum of March 29, 1979, re: PP#8F2121).

The formulation proposed for use on strawberries is Ridomil® 2E, an emulsifiable concentrate that contains 2 lb active ingredient (ai) per gallon (EPA Registration No. 100-607). All ingredients in this formulation are cleared under 40 CFR 180.1001.

Proposed Use on Strawberries

For control of vascular collapse (Phytophthora cactorum) on annual strawberries, apply metalaxyl at a rate of 1 lb ai/A in 20 to 200 gal water after transplanting. A second application at 1 lb ai/A should be applied during the winter, and a third application may be made midway through the harvest season.

For control of red stele (Phytophthora fragariae) and leather rot (P. cactorum) on perennial strawberries, apply metalaxyl at a rate of 1 lb ai/A in 20 to 200 gal water at transplanting or before growth starts in early spring, and make another application in the fall when conditions are favorable for red stele.

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Application of metalaxyl to strawberry plants can be made using ground equipment or through irrigation systems.

The proposed label makes no mention of a preharvest interval (PHI), thus, allowing harvesting on the day of application (i.e., PHI = 0 days).

Nature of the Residue

No new metabolism studies have been submitted with the subject petition. Radiolabel metabolism studies have been reviewed by RCB for potatoes, grapes, and lettuce (see G. Makhijani memorandum of March 29, 1979, re: PP#8G2121 and P. Errico memorandum of March 9, 1982, re: PP#1F2500), and for spinach and lettuce (see N. Dodd memorandum of December 8, 1983, re: PP#2F2762). Metabolism of metalaxyl in plants involves oxidation of the ring methyl to benzyl alcohol and/or benzoic acid, hydroxylation of the phenyl ring, hydrolysis of the methyl ester, cleavage of the methyl ether, N-dealkylation and subsequent conjugation of some of the metabolites. Based on these studies, RCB has previously concluded that the nature of the residue in plants is adequately understood and the residues of concern consist of the parent metalaxyl and its metabolites (free plus conjugates) containing the 2,6-dimethyl-aniline moiety, and N-[(2-hydroxymethyl)-6-methylphenyl]-N-(methoxyacetyl)alanine, methyl ester.

Animal metabolism of metalaxyl is discussed in RCB reviews of PP#8G2121 (goats and rats) - see G Makhijani memorandum of March 29, 1979, and PP#1F2500 - see P. Errico memorandum of July 16, 1982. Based on these reviews, RCB has previously concluded that the residues of concern in meat and milk are the same as those of concern in plant commodities.

Analytical Methodology

The residue data submitted with the subject petition were generated using Ciba-Geigy Method No. AG-345 entitled "Improved Method for the Determination of Total Residues of Metalaxyl in Crops as 2,6-Dimethylaniline" dated December 12, 1982. This method successfully completed a method trial in conjunction with PP#'s 3F2918 and 3F2919 (see K. Arne memorandum of August 2, 1984).

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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 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 72 to 103 percent (average of 20 samples = 83%). All controls (n = 19) were reportedly < 0.05, except for one sample (0.07 ppm). In any case, this one value is well below the proposed 5 ppm metalaxyl tolerance for strawberries.

RCB concludes that adequate analytical methodology is available for enforcement of the proposed 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 1 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. Thus, adequate storage stability data are available to support the strawberry residue data submitted with this petition.

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Residue field studies were conducted during the 1982/1983 growing seasons in the States of California (5 studies), Louisiana (1 study), and Maryland (1 study).

According to Agricultural Statistics 1984 (a USDA publication), California accounted for approximately 71 percent of the 1982 United States spring strawberry production (6.27 million cwt), while the Pacific Northwest States of Oregon and Washington accounted for 9.8 percent, the Northeast States of New York, New Jersey, and Pennsylvania accounted for 3.2 percent, and the North Central States of Michigan and Ohio accounted for 4.4 percent. Florida accounted for 100 percent of the 1982 winter strawberry production (0.98 million cwt).

Strawberry plants received from two to four applications at 1.0 lb ai/A, or two to three applications at 2.0 lb ai/A, while PHI's ranged from 0 to 68 days (note: proposed use allows a maximum of three applications at a rate of 1.0 lb ai/A with a zero-day PHI).

The reported results, corrected for method recovery, are tabulated below:

State	Number of Applications	Rate (lb ai/A)	PHI (days)	Maximum Residue (ppm)
CA (Ventura)	2	1.0	21-35	0.47
	3	1.0	0-20	0.28
	2	2.0	21-35	0.40
	3	2.0	0-20	0.52
CA (Santa Cruz)	2	1.0	68	0.23
	2	2.0	68	0.32
MD	3	1.0	40-54	0.24
CA (Santa Cruz)	3	1.0	0-20	0.70
CA (Fresno)	3	1.0	21-35	1.19
	4	1.0	0-20	1.90
CA (Santa Cruz)	2	1.0	21-35	0.52
	3	1.0	0-21	3.43
	2	2.0	21-35	1.14
	3	2.0	0-21	9.1
LA	2	1.0	21-35	0.54
	2	2.0	21-35	0.58

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RCB's Comments/Conclusions re: Residue Data

RCB concludes that the residue data do not support the proposed use on strawberries for the following reasons:

- a. Three out of seven field trials (including both non-CA studies) do not reflect the proposed zero-day PHI; CA = 68 days, MD = 40 to 54 days, LA = 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 (three applications at 1.0 lb ai/A) and minimum PHI (zero-days).

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

Residue in Meat, Milk, Poultry, and Eggs

Since strawberries are not considered an animal feed item, there is little likelihood of secondary residues occurring in meat, milk, poultry, and eggs as a result of the proposed metalaxyl use on strawberries.

Other Considerations

An International Residue Limit Status sheet is included with this review as Attachment 1. Since Codex, Canada, and Mexico have no established limit/tolerance covering residues of metalaxyl in/on strawberries, there is no compatibility problem.

- Attachment 1: International Residue Limit Status sheet
Attachment 2: EPA's Revised Draft Policy Statement on Minor Uses of Pesticides (OPP-30099)

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cc: With Attachments 1 and 2 - PM #21 only
cc: With only Attachment 1 - TOX, R.F., EAB, EEB, FDA,
Reviewer - Firestone, PP#6F3337,
PMSD/ISB

RDI:JHOnley-2/10/86:RDSchmitt-2/10/86

RCB:TS-769C:MPFirestone:CM#2:RM 800b:557-1991
typed by KENCO-2/19/86:edited by mpf-2/20/86

Attachment 1

INTERNATIONAL RESIDUE LIMIT STATUS

J. Does 1/16/86CHEMICAL: metolaxylPETITION NO.: 6F3337CCPR NO.: 138REVIEWER: Michael P. FirestoneCodex Status☐ No Codex Proposal Step
6 or above

Residue (if Step 9): _____

metolaxyl ⁴Proposed U.S. TolerancesResidue: metolaxyl and its metabolites containing
the 2,6-dimethylaniline moiety, and N-
(2-hydroxyethyl-6-methyl-phenyl)-N-methoxy-
acetyl) alanine methyl ester each expressed
as metolaxyl.Crop(s) Limit (mg/kg)none (on strawberries)Crop(s) Tol. (ppm)strawberries 5.0CANADIAN LIMIT

Residue: _____

MEXICAN TOLERANCIA

Residue: _____

Crop(s) Limit (ppm)none (on strawberries)Crop(s) Tolerancia (ppm)none

Notes:

step 6 - JMPR has recommended that MRLs on other
commodities be re-examined on basis of di-
methylaniline moiety.p. 1 of 1