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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCESMEMORANDUM

SUBJECT: PP#6F3330 (RCB #312). Metalaxyl on Asparagus.
Evaluation of Analytical Methods and Residue
Data (Accession Numbers 260562 and 260563)

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Hazard Evaluation Division (TS-769C)

TO: Henry M. Jacoby, PM 21
Fungicide-Herbicide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

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

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 asparagus at 7.0 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 are pending on several crops.

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 asparagus. 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 asparagus.
3. Residue Chemistry Branch (RCB) concludes that the total metalaxyl residue level in/on asparagus will not exceed the proposed 7 ppm tolerance when treated according to the proposed use (i.e., maximum of two applications at a rate of 1.0 lb ai/A; 0-day PHI).
4. Since asparagus (butts and trimmings) are not considered an animal feed item (see J. Wolff memorandum of March 1, 1971 re: Feeding of Asparagus Butts to Livestock), there is little likelihood of secondary metalaxyl residues occurring in meat, milk, poultry, and eggs as a result of the proposed use of metalaxyl on asparagus.
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 asparagus, there is no compatibility problem.

Recommendation

RCB recommends for the proposed 7.0 ppm metalaxyl tolerance on asparagus, Toxicology Branch and Exposure Assessment Branch considerations permitting.

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 asparagus 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 Asparagus

For control of crown rot and spear rot on asparagus caused by Phytophthora spp., apply metalaxyl at a rate of 1.0 lb ai/A in a minimum of 10 gal water over asparagus beds. In cutting beds, make one application 30 to 60 days before the first cutting. For additional control, a second application can be made just before harvest. In new plantings, one application of metalaxyl can be made after planting seedlings or after covering 1-year-old crowns.

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 underwent a method trial in conjunction with PP#'s 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 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, asparagus 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 from 0.05 to 2.0 ppm metalaxyl, recoveries from asparagus ranged from 76 to 88 percent (average of 7 samples = 81%). All controls were reportedly < 0.05 ppm (n=6) except for one control sample possibly contaminated (0.19 ppm). In any case, the single high control value is well below the proposed 7.0 ppm metalaxyl tolerance.

RCB concludes that adequate analytical methodology is available for enforcement of the proposed metalaxyl tolerance for asparagus.

Residue Data

Asparagus samples analyzed in conjunction with this petition were stored from 5 to 10 months under frozen conditions prior to analysis. Storage stability studies of metalaxyl (parent plus metabolites) 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 residue data submitted with this petition.

Residue field trials were conducted during the 1983 growing season in the States of California, Washington, Iowa, North Carolina, Michigan and New Jersey (note: CA, WA, and MI alone accounted for approximately 95% of the total U.S. 1979 production of asparagus).

Asparagus beds received two applications of metalaxyl at either 1.0 lb ai/A (maximum proposed rate) or 2.0 lb ai/A (2X rate). The first application occurred before the spears emerged in the spring or at ground thaw while the second application was made at harvest. Asparagus samples were harvested 0, 7, and 14 days after the second application (note: the proposed minimum PHI is 0 days). The reported residue data (corrected for method recovery) are tabulated below:

State	Application Rate (lb ai/A)	Maximum Total Metalaxyl Residue (ppm) PHI = 0 days	7 days	14 days
CA	1.0	0.57	< 0.05	< 0.05
WA	1.0	4.98	0.18	< 0.05
WA	2.0 (2X)	3.55	0.26	< 0.05
IA	1.0	1.47	0.10	< 0.05
NC	1.0	4.85	0.13	< 0.05
MI	1.0	4.2	---	---
MI	2.0 (2X)	4.3	---	---
NJ	1.0	5.01	< 0.05	< 0.05

Based on the above data, RCB concludes that total metalaxyl residue levels will not exceed the proposed 7 ppm tolerance in/on asparagus treated according to the proposed use (i.e., maximum of two applications at a rate of 1.0 lb ai/A, 0-day PHI).

Residues in Meat, Fat, Milk, Poultry, and Eggs

Since asparagus (butts and trimmings) are not considered an animal feed item (see J. Wolff memorandum of March 1, 1971 re: Feeding of Asparagus Butts to Livestock), there is little likelihood of secondary residues occurring in meat, fat, milk, poultry, and eggs as a result of the proposed use.

Other Considerations

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

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Attachment 1: International Residue Limit Status Sheet

cc: R.F., Circu, Reviewer, TOX, EAB, EEB, PETITION NO. 6F3330
FDA, PMSD/ISB

RDI:Section Head:J.H.ONLEY:Date:1/31/86:RDSchmitt:Date:1/31/86

TS-769:Reviewer:M.Firestone:CM#2:RM:00:557-7484

KENDRICK CONTRACT TYPING:94515:C.Disk:eae:DATE:2/4/86

Attachment 1:

f. Jones
1/2/88

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL: metolaxyl

PETITION NO.: 6F3330

CCPR NO.: _____

REVIEWER: Michael P. Firestone

Codex Status

No Codex Proposal Step 6 or above

Residue (if Step 9): _____

parent only

Crop(s) _____ Limit (mg/kg) _____

none (on asparagus)

Proposed U.S. Tolerances

Residue: metolaxyl and its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester each expressed as metolaxyl
Crop(s) _____ Tol. (ppm) _____

asparagus 7.0

CANADIAN LIMIT

Residue: _____

Crop(s) _____ Limit (ppm) _____

none (on asparagus)

MEXICAN TOLERANCIA

Residue: _____

Crop(s) _____ Tolerancia (ppm) _____

none

Notes: