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

OCT 31 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: **PP#1E4024. Metalaxyl on cranberries. Evaluation of residue data and analytical methodology. MRID # 419964-01. CBTS # 8582. DP Barcode D168812. HED # 1-2396.**

FROM: José J. Morales, Chemist
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THROUGH: Elizabeth Haeberer, Section Head
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TO: Hoyt Jamerson, PM 43
Registration Division (H7505C)
and
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IR-4 and the Experimental Station of New Jersey, is requesting a tolerance for residues of metalaxyl and its metabolites in or on cranberries at 4.0 ppm. Tolerances are established for the 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-methyl)-N-(methoxyacetyl)-alanine methylester, each expressed as metalaxyl, on various racs and commodities of animal origin from 0.02 ppm to 20 ppm (40 CFR 180.408).

Food additive tolerances of 1.0 ppm in wheat milling fractions to 7.0 ppm in citrus oil are reported in 40 CFR 185.4000. Feed additive tolerances of 0.4 ppm in wet apple pomace to 20 ppm in dry tomato pomace are established in 40 CFR 186.4000.

CONCLUSIONS

1. The manufacturing process of technical grade of metalaxyl has been adequately described. Also, we do not foresee any residue problems from impurities in the technical.

2. The proposed label reflects ground application only for formulation 2E. However, residue data submitted represents both ground and aerial application. CBTS would have no objection to the addition of the aerial application use to the label.

3a. The nature of the residue in plants is adequately understood. The residue of concern is metalaxyl, [N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester], and its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methyl)-N-(methoxyacetyl)-alaninemethylester, each expressed as metalaxyl.

3b. Since cranberry is not an animal feed item, no secondary residues in animals are anticipated from the proposed use.

4. Adequate and validated enforcement methods are available for metalaxyl and its metabolites in PAM II, equivalent to CIBA-GEIGY method AG-395, to support the proposed tolerance.

5. The storage stability data are adequate for the proposed tolerance in/on cranberries.

6. We can draw no conclusion concerning the adequacy of the proposed tolerance on cranberries until the petitioner resolves the following concerns: a) why are residue levels from aerial applications of Ridomil 5G higher than those from ground application?, b) why in the Washington field trial, are data from 1X application higher than from the 2X application?

7. Adequate geographical representation of residue data has been submitted.

8. An International Residue Limit Status Sheet is attached to this review. There are no Codex, Canadian or Mexican tolerances established for metalaxyl on cranberries. Therefore, we anticipate no compatibility problems.

RECOMMENDATION

CBTS recommends against the proposed tolerance for reasons given in Conclusion 6.

DETAILED CONSIDERATIONS

PRODUCT CHEMISTRY

The manufacture and physical/chemical characteristics of metalaxyl was submitted in PP#1F2500 and discussed in P. Errico's memo of 3/9/82. There are no toxicological concerns for any of metalaxyl impurities.

There are two formulations proposed for use: Ridomil 2E fungicide and Ridomil 5G fungicide. Ridomil 2E fungicide (EPA Reg. No.100-607) is an emulsifiable concentrate containing 25.1% of metalaxyl and 74.9% of inert ingredients. This formulation contains 2 lbs ai/gal or 25.1% w/w ai. Ridomil 5G (EPA Reg. No. 100-628) is a granular formulation containing 5.0% of metalaxyl and 95% of inert ingredients. This fungicide contains 5% w/w of ai.

CBTS concludes that the manufacturing process of technical grade metalaxyl has been adequately described. Also, we do not foresee any residue problems on fruits and vegetables from impurities in the technical (F. Griffith's memo of 9/20/86).

PROPOSED USE

Metalaxyl is a systemic fungicide to control certain diseases caused by members of Oomycetes class fungi. Metalaxyl 2E is used as a soil application for control of phytophtora root rot of cranberries caused by Phytophtora spp. The label specifies application at 1.0 to 1.75 lbs. ai/A as a broadcast soil application. Three applications per crop season are recommended. The first application should be done in the fall after harvest, the second application in the spring and the third application 45 days before harvest. Metalaxyl 2E should be applied using ground equipment. The product should not be applied by air. To avoid possible illegal residues, do not apply more than 5.25 lbs ai/A per growing season.

Metalaxyl 5G is recommended to be used as a soil application for control of phytophtora root rot of cranberries caused by Phytophtora spp. The label specifies application by ground or air at 1.0 to 1.75 lbs. ai/A. Three applications per crop season are recommended. The first application should be done in the fall after harvest, the second application should be done in the spring followed by a third application 45 days before harvest, with a maximum application of 5.25 lbs. ai/A per growing season.

CBTS concludes that the proposed label reflects ground application only for formulation 2E. However, residue data submitted represents both ground and aerial application. CBTS would have no objection to the addition of the aerial application use to the label.

NATURE OF THE RESIDUE

Plants

Data on plant metabolism has been discussed in P. Errico's memo of 3/9/89 and K. Arne's memo of 1/6/83. Radiolabelled studies indicate that metalaxyl is metabolized along the same pathway in lettuce, grapes, tobacco and potatoes. Catabolism of metalaxyl occurs via oxidation of the ring methyl to the alcohol and carboxylic acid, hydroxylation of the phenyl group, cleavage of the methyl ester and methyl ester, n-dealkylation and subsequent conjugation of some of the various breakdown products. Residues of concern in plants are metalaxyl, and its metabolites containing the 2,6-dimethylaniline moiety. Each of these are expressed as metalaxyl.

CBTS concludes that the nature of the residue in plants is adequately understood.

Animals

Since cranberry is not an animal feed item, no secondary residue problems are anticipated from the proposed use.

ANALYTICAL METHODOLOGY

Analytical methodology AG-395 (PP#8F3617/8H554), as previously described in F. Griffith's memo of 11/28/88, was used to determine residues of metalaxyl and its metabolites containing the 2,6-dimethylaniline moiety and N-[2-(hydroxymethyl)-6-methyl phenyl]-N-(methoxyacetyl) alanine methyl ester ("total residues"). Results are expressed as metalaxyl equivalents with a detection limit of 0.05 ppm.

Samples are extracted by refluxing with 80% (v/v) methanol/water for 2 hours. An aliquot of this extract is evaporated, water and methanesulfonic acid added, and the sample is refluxed for 15 minutes. After cooling and addition of water, the extract is basified. Dimethylalinine formed in the reaction is steam distilled and separated in a fused silica capillary column and detected with a nitrogen-phosphorus detector operating in the nitrogen-specific mode.

Method trials appear in P. Jung's memo of 7/9/84 (PP#3F2978). Method AG-395 has undergone successful validation by EPA and it has been accepted by FDA as an enforcement method. The validation of analytical methodology of AG-395 has been demonstrated and reported in CIBA-GEIGY Biochemistry Summary Report ABR-83033.

CBTS concludes that adequate and validated enforcement methods are available for metalaxyl and its metabolites in PAM II, equivalent to CIBA-GEIGY method AG-395, to support the proposed tolerance.

MULTIRESIDUE TESTING

The petitioner has determined recoveries of metalaxyl under FDA multiresidue protocols (G. Otakie's memo of 2/22/91). However, additional multiresidue test information for metabolite CGA-94689 is needed.

RESIDUE DATA

Data from eight field trials were submitted in support of the tolerance proposal on cranberries. Trials were conducted in Massachusetts (2), New Jersey (2), Oregon (1), Washington (1) and Wisconsin (2). These trials were conducted during the 1988 growing season. According to Agricultural Statistics, 1985, these states accounted for 100% of the cranberry grown in the United States.

CBTS concludes that adequate geographical representation of residue data has been submitted.

Ground and aerial treatments were used. Metalaxyl was applied at a maximum 1X use rate, using three applications at a rate of 1.75 lbs. ai/A/grown season. In the New Jersey trials the use rate was of 2.2 lbs. ai/A/grown season (1.3X) for the Ridomil 2E formulation. Cranberries were harvested at random from within the plots 45 to 47 days after the last application of metalaxyl.

After collection, samples were frozen and shipped with dry ice to CIBA-GEIGY corporation, Greensboro, North Carolina. Upon arrival, samples were stored at -20°C. Sample preparation was performed according to FDA Pesticide Analytical Manual, Vol. 1 section 141 and CIBA-GEIGY SOP 7.20, Revision O. After preparation, samples were placed in polyethylene bottles, identified and returned to a freezer within 8 hours after subsampling for analysis. All samples were stored between six and seven months prior to metalaxyl analysis. Metalaxyl and metabolites analysis were conducted using the methodology previously described.

Recovery data were obtained from untreated samples fortified with metalaxyl at levels ranging from 0.05 ppm to 0.5 ppm, with recoveries from 52 to 135% (n=18, mean 85.2%, standard deviation of 20.2%). Submitted chromatograms show well resolved peaks in support of this data.

Residues of metalaxyl were shown to be stable for a minimum of 18 months when stored under -15°C. Data available in commodities like potatoes and tobacco can be found in Registration Standards pp. 20 to 21. Results of freezer stability have been reported in ABR-80028 and ABR-86044. All cranberry samples were stored between six and seven months prior to metalaxyl analysis.

CBTS concludes that available storage stability data of metalaxyl is adequate.

Table I summarize the quantity of residues found in cranberries at a PHI of 45, 46, and 47 days. As can be seen from the table the maximum 1X total metalaxyl residue in cranberries receiving 1X treatment regime was 3.8 ppm at a 46 day PHI. Also, residue levels resulting from Ridomil 2E applications were somewhat higher than those obtained from Ridomil 5G applications. Exaggerated 2X applications were made in four field tests for purpose of residue comparison, and 2X residues were generally higher. In the Washington trial, residue levels in the 1X Ridomil 2E treatment samples were substantially higher than the residues from the 2X Ridomil 2E treatment samples i.e., 3.8 ppm vs. 0.97 ppm. These results suggest an inadvertent sample switch in the field. In the New Jersey trial 1.3X and 2.1X application of Ridomil 2E was used.

Table I. Metalaxyl residues in cranberries resulting from applications of Ridomil 2E or Ridomil 5G.

Field Test	Formulation	Rate[1]	Method of Application[2]	PHI	Total Metalaxyl Residue (ppm)[3]
OR	2E	1X	G	45	0.39
	5G	1X	G	45	0.15
WI	2E	1X	G	45	0.66
		2X	G	45	1.1
	5G	1X	G	45	0.16
WI	2E	1X	G	45	0.65
WA	5G	1X	G	45	0.06
NJ	2E	1.3X	G	46	0.20
		2.1X	A	46	0.14
	5G	1X	G	46	0.11
NJ	2E	1.3X	G	46	0.25
		2.1X	A	46	0.07
	5G	1X	G	46	<0.05
WA	2E	1X	G	46	3.8
		2X	G	46	0.97
	5G	1X	G	46	<0.05
MA	2E	1X	G	47	0.95
		2X	G	47	1.3
	5G	1X	G	47	<0.05
		1X	A	47	0.28
MA	2E	1X	G	47	0.35
	5G	1X	G	47	0.06
		1X	A	47	0.14

1. 1X - 3 applications at a rate of 1.75 lbs. ai/A
   1.3X - 3 applications at a rate of 2.2 lbs. ai/A
   2X - 3 applications at a rate of 3.5 lbs. ai/A
2. G - ground A - aerial
3. 2,6-dimethylaniline reported as metalaxyl equivalent.

We can draw no conclusion concerning the adequacy of the proposed tolerance on cranberries until the petitioner resolves the following concerns: a) why are residue levels from aerial applications of Ridomil 5G higher than those from ground application?, b) why in the Washington field trial, are data from 1X application higher than from the 2X application?

OTHER CONSIDERATIONS

An International Residue Limit (IRL) Status Sheet is appended to this review. There are no Codex, Canadian or Mexican limits established for metalaxyl on cranberries. Therefore, no compatibility problem exist.

Attachment: International Residue Limit Status Sheet.

cc: SF, RF, Circu., C. Furlow (PIB/FOD), José J. Morales, E. Haeberer, PP#1E4024.

H7509C: Reviewer (JJM): CM#2: Rm 812-C: 557-2990: typist (JJM): 10/20/91.

RDI: E. Haeberer (10/30/91): R. Loranger (10/30/91)

J. Morales 10/24/91

Attachment:

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INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Metalaxyl

CODEX NO. _____

CODEX STATUS:

[✓] No Codex Proposal Step 6 or Above (on cranberry)

Residue (if Step 8): _____

Metalaxyl per se on other commodities

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 1E4024

DEB Reviewer J. MORALES

Residue: Metalaxyl

Crop(s)	Limit (mg/kg)
Cranberry	4.0 ppm

CANADIAN LIMITS:

[✓] No Canadian Limit (on cranberry)

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

[✓] No Mexican Limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES

Form Revised 1989