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OPP OFFICIAL
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

AUG 03 1989

MEMORANDUM

SUBJECT: PP#8F3698: Metalaxyl; Tolerances for Metalaxyl for the Crop Grouping Root and Tuber Vegetables. Evaluation of Residue Data and Analytical Methodology. MRID Nos. 408383-01 to 408383-03; DEB Nos.4788 to 4791.

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Joel Garbus

THRU: R. D. Schmitt, Ph.D., Chief
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CIBA-GEIGY Corporation, Greensboro, NC, requests that permanent tolerances be established for the combined residues of metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester] and its metabolites containing the 2,6-dimethylaniline moiety and N-(2-hydroxymethyl-6-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester, each expressed as metalaxyl equivalents, in or on the root and tuber vegetable grouping as follows:

Root and Tuber Vegetable Tops	15.0 ppm
Root and Tuber Vegetable Roots	0.5 ppm

Residues of metalaxyl in processed commodities could result from this usage. A food/feed additive tolerance request to increase the tolerance to 4 ppm for metalaxyl residues has been submitted for sugar beet molasses (PP#8H5554).

The petitioner also requests that the registration of Ridomil MZ58, a fungicide end-use product consisting of metalaxyl and mancozeb, be amended to allow for its application to carrots.

The representative commodities for the root and tuber vegetable group are potatoes, carrots, radishes, and sugar beets.

The representative commodities for the leaves of the root and tuber vegetable (human food or animal feed) group are turnips and sugar beets.

Of these commodities, tolerances are established [40 CFR 180.-408(a)] 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-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester in or on beets, beet tops, sugar beets, and sugar beet tops at 0.1 ppm and in or on potatoes at 0.5 ppm.

There are no rotational crop tolerances for the root and tuber vegetable group. (There is a rotational tolerance for wheat.) There are plant back restrictions of 9 months for root and tuber vegetables for Ridomil MZ58 and 12 months for Ridomil 2E.

A food additive tolerance has been established for residues of metalaxyl and its metabolites in processed potatoes (including chips) at 4.0 ppm [40 CFR 185.4000 (a)].

Feed additive tolerances have been established for residues of metalaxyl and its metabolites for several rac processing products including sugar beet molasses at 0.1 ppm [40 CFR 186.4000(a)].

With respect to a few of the representative commodities for the root and tuber vegetable group and the leaves of the root and tuber vegetable (human food or animal feed) group, tolerances of 2 ppm are established for residues of mancozeb in or on carrots and sugar beets and of 65 ppm in or on sugar beet tops [40 CFR 180.176]. An interim tolerance of 1.0 ppm is established for mancozeb in or on potatoes [40 CFR 180.319].

A Registration Standard (non-food use only) has been issued for metalaxyl (9/15/81). A FRSTR (both food and non-food use) for metalaxyl was issued on 6/22/87.

Conclusions

1a. The nature of the residue in plants is understood. The residue of concern consists of metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester, each expressed as metalaxyl equivalents.

1b. According to the FRSTR, the nature of the residue in animals is not understood. The residues currently regulated in animals consist of metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-dimethylphenyl)-N-

(methoxyacetyl)-alanine methyl ester, each expressed as metalaxyl equivalents. We continue to recommend regulating these residues in meat, milk, poultry, and eggs for this petition while the animal metabolism requirements are being satisfied for the FRSTR.

2a. Section B, the proposed use on the root and tuber vegetable group, includes one at-plant and up to four foliar applications of the Ridomil MZ58 formulation (0.8 lbs ai/A). This formulation contains both metalaxyl and mancozeb. Mancozeb does not have tolerances established on the representative crops nor group tolerances for the root and tuber vegetable group and for the leaves of the root and tuber vegetable (human food or animal feed) group. The petitioner notes in their cover letter that they also are applying for an amended registration to add only carrots to the registration for the Ridomil MZ58 formulation.

2b. We cannot accept the proposed use in Section B as written as there are no tolerances established for mancozeb for the root and tuber vegetable group and for the leaves of the root and tuber vegetable (human food or animal feed) group. If the use is subsequently restricted to only those crops with mancozeb tolerances, the use patterns will be too dissimilar to allow us to recommend for metalaxyl tolerances on these same crop groups. (See exceptions to this for carrots and potatoes under 2d below.)

2c. Alternatively, the petitioner could request crop group tolerances only for the proposed soil use of metalaxyl, but field residue data must be submitted. The field residue data submitted in this petition includes the proposed soil use and foliar uses. Because the additional foliar use is expected to lead to higher residues of metalaxyl than necessary on the leaves of root and tuber vegetables, compared to what would be expected from only the soil treatment, we are not able to recommend for appropriate tolerances for the soil treatment alone.

2d. The exception to the above discussions in conclusions 2b and 2c is the proposed soil treatment and foliar use on carrots and potatoes. Because the tops of carrots and potatoes are not considered food or feed items at the present time (see 40 CFR 180.1 (j) 6 for carrots), we can consider a specific request for tolerances for metalaxyl on carrots and potatoes for both the proposed soil treatment and foliar application with Ridomil MZ58 if additional field residue data are submitted from the states of MI or WI, OH, FL, and MN for carrots and CO, ID, and WI for potatoes. The residue data should reflect the maximum rates and minimum PHI's.

2e. An appropriate residue determination for this use on sugar beets is being considered by DEB in the pending PP#8F3617.

3. Adequate and validated analytical methodology is available for metalaxyl and its metabolites.

4. DEB defers to EFGWB as to the need for rotational crop studies resulting from the use of metalaxyl/mancozeb on root and tuber vegetables.

5. In the absence of requested animal metabolism studies, currently established tolerances for animal tissues are sufficient to accommodate secondary residues in meat, milk, poultry, and eggs arising from this proposed use of metalaxyl on commodities of the root and tuber vegetable group and the leaves of the root and tuber vegetable (human food or animal feed) group.

6. There are no international residue limits for metalaxyl or its metabolites for the root and tuber vegetable group and the leaves of the root and tuber vegetable group as a whole. There are Codex limits for metalaxyl, per se, of 0.1 ppm for carrots, and 0.05 ppm for potatoes and sugar beets. There are Canadian limits for metalaxyl, per se, of 0.1 on potatoes. There are no Mexican limits for metalaxyl in/on commodities of the root and tuber vegetable group and the leaves of the root and tuber vegetable group.

Recommendation

DEB recommends against the proposed tolerances for the root and tuber vegetable group and the leaves of the root and tuber vegetable (human food or animal feed) group for metalaxyl for the reasons stated in conclusions 2a, 2b, 2c, and 2e.

Manufacture and Formulation

The manufacture and the physical/chemical characteristics of metalaxyl have been submitted and reviewed in establishing existing tolerances. (See DEB review of PP1F2500, P. Errico, 3/9/1982.) These data are cited by reference in the current submission.

Proposed Use

Metalaxyl, a systemic fungicide, is used to control damping-off and root rot caused by Pythium and Phytophthora spp. of the Oomycete class fungi.

The label states that this use on root and tuber vegetables includes but is not limited to artichoke, beet (sugar and table), carrot, cassava, chicory, ginger, ginseng, horseradish, parsnip, potato, radish, rutabaga, salsify, sweet potato,turnip, and yams.

As a preplant or at-planting application apply 1-2 lbs ai/A of metalaxyl.

For foliar application use metalaxyl/mancozeb (Ridomil MZ58). Begin when conditions are favorable for disease but before actual

infection and continue at 14 day intervals. Use 0.87 to 1.16 lbs ai/A of metalaxyl/mancozeb. (This is equivalent to 0.15 to 0.2 lbs ai/A of metalaxyl and 0.72 to 0.96 lbs ai/A of mancozeb.) The higher rates are to be used under heavy disease pressures. No more than 4 application should be made per season with the last at least 7 days before harvest.

Treated areas can be immediately replanted to root and tuber vegetables.

The statement that the use on root and tuber vegetables includes the major commodities in these groups "but is not limited to" them is not clear. If group tolerances are granted, the tolerances are limited to the members of the group as defined in section 180.34 (f) 9 (i) and (ii). If uses are requested on commodities other than those defined as in the group, individual tolerances are needed for these commodities. The statement on the proposed label would be acceptable if the phrase "but is not limited to" were to be removed.

Nature of the Residue:

Detailed discussions of the metabolism of metalaxyl by plants and animals have been submitted in support of currently established tolerances. (See DEB reviews of 1F2500, P. Errico, 3/9/82 and of 2F2762, K. Arne, 1/6/83.) Plant metabolism studies were carried out with potatoes, lettuce, tobacco, and grapes. It is expected that metalaxyl applied to root and tuber vegetables will be metabolized via the same pathways demonstrated for other crops with established tolerances.

The residue of concern in or on root and tuber vegetables will consist of metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester, each expressed as metalaxyl equivalents.

The animal metabolism of metalaxyl was considered to be similar to that in plants. (See DEB reviews of 1F2500, P. Errico, 3/9/82 and of 2F2762, K. Arne, 1/6/83.) The residue of concern in animal tissues was considered to consist of metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester, each expressed as metalaxyl equivalents. However, the FRSTR of 6/22/87 concluded that the animal metabolism of metalaxyl is not adequately known and that additional animal metabolism studies are required.

We continue to recommend regulating these residues in meat, milk, poultry, and eggs for this petition while the animal metabolism requirements are being satisfied for the FRSTR.

Analytical Methods

CIBA-GEIGY analytical method AG-395 was used to determine total metalaxyl residues in root and tuber vegetables. This method determines residues as 2,6-dimethyl aniline and reports residues as metalaxyl equivalents. This is the enforcement method of PAM II.

The method and its validation have been discussed and reviewed in previous DEB memoranda. Storage stability studies for residues of metalaxyl and its metabolites have also been reviewed and accepted. (See DEB reviews of 1F2500, P. Errico, 3/9/82 and of 2F2762, K. Arne, 1/6/83)

Enviro-Bio-Tech methods were used to analyze for the residues resulting from mancozeb.

Adequate analytical methodology is available to enforce the requested tolerance for metalaxyl and its metabolites for the proposed use.

Residue Data (Root and tuber vegetables)

Twenty residue trials were conducted with the representative root and tuber vegetables, carrots, potatoes, radishes, and sugar beets, in ten states, CA, ME, NB, ND, MN, OH, WA, NY, TX, and FL. Carrots were grown and treated in CA, NY, WA, and TX (69% of national crop); potatoes were grown and treated in CA, ME, ND, WA, and FL (35% of national crop); sugar beets were grown and treated in WA, CA, MN, TX, OH, and NE (49% of national crop); radishes were grown and treated in CA, NY, and FL. No residue data on turnip tops were submitted.

Ridomil 2E, an emulsifiable formulation of metalaxyl, was applied at the proposed maximum rate of 2.0 lb ai/A to root and tuber vegetables at planting. Ridomil MZ58, a formulation containing metalaxyl and mancozeb, was applied up to four times to carrots, potatoes, and sugar beets, for a total of 0.8 lbs metalaxyl, and two times to radishes, for a total of 0.4 lbs metalaxyl. Total metalaxyl applied to crops were 2.8 lbs for carrots, potatoes, and sugar beets and 2.4 lbs to radishes. Crops were harvested 7 to 9 days after the last application.

Samples were frozen and shipped to CIBA-GEIGY at Greensboro NC and stored frozen until analyzed. Samples from 18 of the 20 studies were analyzed within 18 months, the period for which storage stability has been demonstrated. Two sets of samples were analyzed 19 and 20 months respectively after harvest. Storage stability is assumed for these additional months.

Recoveries from fortified samples averaged 90.7 ± 17%.

Residues in control samples ranged from below the limit of detection (0.05 ppm) for potatoes to 0.69 ppm for carrot tops.

Residues in root and tuber vegetables resulting from the recommended label applications of metalaxyl and metalaxyl/mancozeb were as follows:

Location	Matrix	PHI	Residues (ppm) as Metalaxyl Equivalents
Potato Tubers			
California	Mature Tuber	7	0.06, 0.07
Maine	Mature Tuber	8	<0.05, <0.05
North Dakota	Mature Tuber	8	0.19, 0.12
Washington	Mature Tuber	7	<0.05, <0.05
Florida	Mature Tuber	9	0.10, 0.11
Carrots			
New York	Tops	7	1.5, 2.9
California	Tops	7	6.7, 7.1
Washington	Tops	7	3.6, 3.3
Texas	Tops	7	1.7, 1.6
Carrots			
New York	Roots	7	<0.05, <0.05
California	Roots	7	0.22, 0.15
Washington	Roots	7	<0.05, 0.06
Texas	Roots	7	<0.05, <0.05
Radishes			
Florida	Tops	7	9.9, 13
New York	Tops	7	1.4, 1.8
California	Tops	7	5.7, 6.2

Location	Matrix	PHI	Residues (ppm) as Metalaxyl Equivalents
Radishes			
Florida	Roots	7	0.24, 0.29
New York	Roots	7	0.23, 0.28
California	Roots	7	0.25, 0.35
Sugar Beets			
Washington	Tops	7	4.4, 3.2
California	Tops	7	3.8, 4.2
Minnesota	Tops	7	1.0, 1.5
Texas	Tops	7	2.3, 2.2
Ohio	Tops	8	0.64, 1.1
Nebraska	Tops	7	1.5, 2.1
Sugar Beets			
Washington	Roots	7	0.10, 0.10
California	Roots	7	0.10, 0.07
Minnesota	Roots	7	0.11, 0.09
Texas	Roots	7	0.15, 0.20
Ohio	Roots	8	<0.05, <0.05
Nebraska	Roots	7	0.10, 0.06

Location	Matrix	PHI	Residue (ppm) as Metalaxyl Equivalents	
			1X	2X rate

Potato Processing Fractions

Location	Matrix	PHI	Residue (ppm) as Metalaxyl Equivalents	
			1X	2X rate
Washington	Mature Tuber	7	<0.05	<0.05
	Wet Peel	7	<0.05	<0.05
	Sliced and Peeled	7	<0.05	<0.05
	Wash Water	7	<0.05	<0.05
	Chips	7	<0.05	<0.05
	Steamed Peel	7	<0.05	<0.05
	Dry Peel	7	<0.05	<0.05
	Flakes	7	<0.05	<0.05

Sugar Beet Processing Fraction

Nebraska	Roots	7	0.036	0.07
	Cassettes	7	<0.05	<0.05
	Pulp	7	<0.05	<0.05
	Molasses	7	0.25	0.26
	Sugar	7	<0.05	<0.05

When 2x the proposed application rates were used, residues ranged from <0.05 ppm to 0.28 ppm in/on potatoes, from 0.26 ppm to 7.1 ppm in/on carrot tops, and from 0.06 ppm to 0.90 ppm in/on carrot roots. Single trials at 2X the application rates were conducted with radishes and sugar beets. At these rates, 14 ppm were found in/on radish tops, 0.57 ppm in/on radish roots, 3.2 ppm in/on sugar beet tops, and 0.90 ppm in/on sugar beet roots.

Residue data were also submitted from CA, ND, WA, and FL for potatoes at 0 day PHI with reported residues of metalaxyl at <0.05 ppm to 0.51 ppm at the 1X rate and 0.06 ppm to 0.28 ppm at the 2X rate.

The maximum residues at the proposed use for metalaxyl found in the representative root and tuber vegetables were 13 ppm for radish tops and 0.35 ppm in radish roots.

No residues of metalaxyl were found in potato processing fractions. A 7-fold concentration of metalaxyl residues was found for sugar beet molasses processed from sugar beet roots treated at the label rate. (See PP#8F3617.) As a separate petition request, the registrant is asking for a 4 ppm food/feed additive tolerance for

sugar beet molasses. An appropriate residue determination for this use on sugar beets will be considered in our review of PP#8F3617.

For carrots, potatoes, sugar beets and sugar beet tops the residues of mancozeb metabolites were within the established tolerances.

The proposed use on the root and tuber vegetable group includes one at-plant and up to four foliar applications of the Ridomil MZ58 formulation (0.8 lbs ai/A). The residue data given above was generated using this formulation. This formulation contains both metalaxyl and mancozeb. Mancozeb does not have tolerances established on the representative crops nor group tolerances for the root and tuber vegetable group and for the leaves of the root and tuber vegetable (human food or animal feed) group. The petitioner notes in their cover letter that they also are applying for an amended registration to add only carrots to the registration for the Ridomil MZ58 formulation.

We cannot accept the proposed use as there are no tolerances established for mancozeb for the root and tuber vegetable group and for the leaves of the root and tuber vegetable (human food or animal feed) group. If the use is subsequently restricted only to those crops with mancozeb tolerances, the use patterns will be too dissimilar to allow us to recommend for metalaxyl tolerances on these same crop groups. (See exceptions to this for carrots and potatoes below.)

The petitioner could request crop group tolerances only for the proposed soil use of metalaxyl, but appropriate field residue data must be submitted. The field residue data submitted in this petition includes the proposed soil use and foliar uses. Because the additional foliar use is expected to lead to higher residues of metalaxyl on the leaves of root and tuber vegetables, compared to what would be expected from only the soil treatment, we are not able to recommend for appropriate tolerances for the soil treatment alone.

The exception to the above discussions is the proposed soil treatment and foliar use on carrots and potatoes. Because the tops of carrots and potatoes are not considered food or feed items at the present time (see 40 CFR 180.1 (j) 6 for carrots), we can consider a specific request for tolerances for metalaxyl on carrots and potatoes for both the proposed soil treatment and foliar application with Ridomil MZ58 if additional field residue data are submitted from the states of MI or WI, OH, FL, and MN for carrots and CO, ID, and WI for potatoes. The residue data should reflect the maximum rates and minimum PHI's.

An appropriate residue determination for this use on sugar beets is being considered by DEB in the pending PP#8F3617.

Meat, Milk, Poultry, and Eggs

The petitioner has calculated the dietary burden of metalaxyl and its metabolites that would be presented to livestock consuming diets containing treated alfalfa. For this purpose, the petitioner has constructed a theoretically possible diet for cattle that would be comprised of components bearing the greatest levels of residue at tolerance values. For cattle the diet would be:

Peanut Hay	at 20.0 ppm	as 60% of diet	= 12.0	ppm
Dried Tomato Pomace	at 20.0 ppm	as 25% of diet	= 5.0	ppm
Root and Tuber Tops	at 15.0 ppm	as 15% of diet	= 2.25	ppm

for a total of 19.25 ppm

The results of feeding studies with cattle at high levels (15 and 75 ppm) were submitted in conjunction with PP#1F2500. Based upon the results of these feeding studies, we can calculate the levels of residue of metalaxyl expected in tissues of cattle and in milk. In all instances, calculated tissue levels (0.044 and 0.023 ppm in muscle, 0.005 ppm in milk) fall below currently established tolerances for meat (0.05 ppm) and milk (0.02 ppm).

Root and tuber vegetables do not constitute a part of poultry diets.

If the required animal metabolism requested by the metalaxyl FRSTR identify no additional metabolites, DEB will conclude that establishing tolerances for the use of metalaxyl on root and tuber vegetables alfalfa will not necessitate the revision of existing tolerances on animal commodities. (Also see comments on the nature of the residue above.) The currently established tolerances for animal tissues are sufficient to accommodate the use of metalaxyl on these commodities.

International Residue Limit Status

There are no international residue limits for metalaxyl or its metabolites for the root and tuber vegetable group and the leaves of the root and tuber vegetable group as a whole. There are Codex limits for metalaxyl, per se, of 0.1 ppm for carrots, and 0.05 ppm for potatoes and sugar beets. There are Canadian limits for metalaxyl, per se, of 0.1 on potatoes. There are no Mexican limits for metalaxyl in/on commodities of the root and tuber vegetable group and the leaves of the root and tuber vegetable group.

cc: PP9F3698, S. File, RF., Circ., Reviewer, PMSD/ISB
RDI: PE:7/27/89:RDS:7/31/89
H7509C:DEB:JG:jg:CM:2:Rm:803:557-1405:7/31/89.

f. 7/31/91

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Metalaxyl

CODEX NO. 138

CODEX STATUS:

☐ No Codex Proposal Step 6 or above

Residue(if Step 8): Metalaxyl per se

Crop(s)	Limit (mg/kg)
carrot	0.1 [1]
potato	0.05
sugar beet	0.05

PROPOSED U.S. TOLERANCES:

Petition No. 8F3698

RCB Reviewer JG

Residue: METALAXYL + Metabolites

Crop(s)	Limit (mg/kg)
ROOT AND TUBER ROOTS GROUP	0.5
ROOT AND TUBER LEAVES GROUP	15

CANADIAN LIMITS:

☐ No Canadian limit

Residue: Metalaxyl per se

Crop(s)	Limit (mg/kg)
potatoes	0.1 [2]

MEXICAN LIMITS:

☐ No Mexican limit

Residue:

Crop(s)	Limit (mg/kg)

NOTES:
1/ Step 5 2/ Negligible residue type limit

Form revised 1986