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

D174355 ? 8th

JAN 15 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 2F04072: 1. Metalaxyl (Ridomil®2E Fungicide, EPA Reg. No. 100-607) in or on members of the Brassica (cole) leafy vegetables crop grouping; evaluation of request for amended registration, analytical method and residue data of mustard greens.

FROM: Mary H. Peters, Chemist
Tolerance Petition Section I
Chemistry Branch I-Tolerance Support
Health Effects Division (H7509C)

THROUGH: Debra Edwards, Ph.D., Chief
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Health Effects Division (H7509C)

TO: Benjamin Chambliss/Susan Lewis, PM Team 21
Fungicide-Herbicide Branch
Registration Division (H7505C)

The Ciba-Geigy Corporation requests establishment of a tolerance for the residues of the fungicide metalaxyl in or on members of the Brassica (cole) leafy vegetables crop grouping at 5.0 ppm.

Tolerances are established for residues of the fungicide metalaxyl (N-(2,6-dimethylphenyl)-N-methoxyacetyl alanine methyl ester) and its metabolites containing the 2,6-dimethylaniline (2,6-DMA) moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)-alanine methyl ester, expressed as metalaxyl equivalents under 40 CFR §180.408 for various raw agricultural commodities including Brassica (cole) leafy vegetables crop group (except broccoli, cabbage, and cauliflower) at 0.1 ppm; broccoli, cabbage, and cauliflower at 2.0 ppm; and leafy vegetables (except Brassica) crop group at 0.1 ppm; and for food and feed additive tolerances under 40 CFR §185.4000 and 40 CFR §186.4000, respectively.

The intent of this petition is to raise the existing tolerances of 0.1 ppm on Brassica leafy vegetables (except broccoli, cabbage, and cauliflower) and 2 ppm on broccoli, cabbage, and cauliflower to 5 ppm on Brassica leafy vegetables. This would permit foliar application to broccoli, Brussels sprouts, cabbage,

and cauliflower. The foliar application is to be with a water soluble bag formulation containing both chlorothalonil and metalaxyl. Residue data for mustard greens are submitted with this petition. Residue data were submitted in a previous petition for cabbage, cauliflower, and broccoli. The representative crops for this grouping are cabbage, broccoli, and mustard greens.

Metalaxyl is a List A chemical and there is a metalaxyl Registration Standard (6/87) as well as a metalaxyl Product Chemistry and Residue Chemistry Registration Standard Update (4/92).

Tolerances are established for residues of the fungicide chlorothalonil (tetrachloroisophthalonitrile) and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile under 40 CFR §180.275 on various raw agricultural commodities including broccoli, Brussels sprouts, cabbage, and cauliflower at 5.0 ppm. There are no established tolerances on meat, milk, poultry, and eggs; or for food or feed additives. Chlorothalonil is a List A chemical and there is a chlorothalonil FRSTR (2/19/88).

A letter dated 12/18/91 from Karen Stumpf, Regulatory Manager, Ciba-Geigy to Ms. Susan Lewis, authorizes the Agency to refer to Ciba-Geigy data in support of these requests.

CONCLUSIONS

1. The manufacturing process of metalaxyl (technical product) has been adequately described.

2a. The nature of metalaxyl residues in plants is adequately understood.

2b. The nature of chlorothalonil residues in plants is not adequately understood. However, for the purposes of this label amendment which includes chlorothalonil in the metalaxyl formulation, CBTS considers chlorothalonil and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile as the residues of concern.

3. There are no animal feed items involved with this petition, therefore, the nature of the residue in animals and the resulting secondary residues in meat, milk, poultry, and eggs is not relevant.

4. Adequate analytical methods are available in PAM for enforcement of tolerances on Brassica (cole) leafy vegetables.

5. CBTS concludes that the lettuce and cabbage storage stability studies indicate some loss in storage of metalaxyl residues that need to be corrected for.

6. The geographical representation for the field trials of metalaxyl on mustard greens is adequate.

7. CBTS requires enough data to determine how corrected metalaxyl residue values were obtained. Uncorrected residue data (ppm of metalaxyl equivalents) or chromatogram data (peak heights, peak areas, etc.) should be submitted for mustard greens.

8. Maximum residues of metalaxyl on mustard greens were 4.7 ppm after correcting for the loss in storage. A tolerance of 5.0 ppm on mustard greens appears to be adequate provided that CBTS accepts the petitioner's method of correction for the existing residue data.

9. Maximum residues of metalaxyl vary between the representative crops mustard greens (at 4.7 ppm) and cabbage (at 0.53 ppm) by more than a factor of five. Therefore, a crop group tolerance is inappropriate for metalaxyl in or on Brassica (cole) leafy vegetables (as per 40 CFR §180.34(f)(5)).

10. Maximum residues of metalaxyl as a result of the soil plus foliar applications were 0.53 ppm for cabbage, 0.87 ppm for cauliflower, and 1.3 ppm for broccoli after correcting for the loss in storage. Therefore, tolerances of 1.0 ppm for cabbage and cauliflower, and 2.0 for broccoli would be appropriate to cover the soil plus foliar uses.

11. The current tolerance of 0.1 ppm on Brussels sprouts as a member of the Brassica (cole) crop group reflects a seed treatment. The petitioner has proposed a tolerance to reflect a foliar application on Brassica (cole) leafy vegetables. Since CBTS cannot recommend in favor of a tolerance for the crop group, the petitioner must propose a tolerance on Brussels sprouts, independent of the current crop group tolerance, if they wish to register the foliar application for use on Brussels sprouts. Translation of the broccoli residue data to Brussels sprouts would indicate that a 2 ppm tolerance for metalaxyl on Brussels sprouts is appropriate.

12. Because of differences in the tolerance expressions and the residue levels between Codex and U.S. data, compatibility is not possible at this time.

RECOMMENDATIONS

CBTS cannot recommend in favor of a crop group tolerance for metalaxyl on Brassica (cole) leafy vegetables because of conclusion 9. Conclusions 8, 10, and 11 address alternatives regarding establishing individual tolerances on the subject crops.

CBTS cannot recommend in favor of a tolerance for metalaxyl on mustard greens because of conclusion 7.

Because of conclusions 10 and 11, CBTS recommends that tolerances of 1.0 ppm for cabbage and cauliflower and 2.0 for Brussels sprouts would be appropriate and should be proposed. The 2.0 ppm tolerance for broccoli should remain the same.

If the petitioner submits the above amendments, they should request that 40 CFR §180.408 reads as follows (amendments are in bold type); or separate tolerances should be delineated for members of the Brassica (cole) crop group:

Brassica (cole) leafy vegetables group [except broccoli, cabbage, cauliflower, **Brussels sprouts, and mustard greens**]	0.1 ppm
Broccoli	2.0 ppm
Brussels sprouts	**2.0 ppm**
Cabbage	**1.0 ppm**
Cauliflower	**1.0 ppm**
Mustard greens	**5.0 ppm**

Note to PM: There is no established tolerance for chlorothalonil in or on mustard greens. If the petitioner wishes to register Ridomil/Bravo®81W for use on mustard greens, a tolerance for chlorothalonil in or on mustard greens will be needed.

DETAILED CONSIDERATIONS

Manufacturing Process and Formulation:

Ridomil®2E (EPA Reg. No. 100-607, Ciba-Geigy Corporation, Greensboro, NC) is an emulsifiable concentrate containing 25.1% active ingredient and 74.9% inert ingredients (2.0 lbs. active ingredient per gallon).

Ridomil/Bravo®81W (EPA Reg. No. 100-658, Ciba-Geigy Corporation, Greensboro, NC) is a wettable powder containing 9% of the active ingredient metalaxyl, 72% of the active ingredient chlorothalonil, and 19% inert ingredients.

The manufacturing process of metalaxyl (technical product) has been adequately described in the Chemistry Branch review of PP#1F2500 (P. Errico, 3/9/82). The TGAI is >95% pure and the impurities are not likely to produce a residue problem.

Proposed Use:

Ridomil®2E (Cole Crops):

Ridomil®2E is to be applied to the soil at planting as a preplant incorporated treatment or as a soil surface spray after planting.

For a preplant incorporated treatment, apply 4-8 pints (1-2 lbs. ai)/treated acre as a broadcast soil application in sufficient water or liquid fertilizer to provide uniform coverage and incorporate in the top two inches of soil. For a soil surface application, apply 4-8 pints (1-2 lbs. ai)/treated acre at planting in sufficient water or liquid fertilizer to provide uniform coverage. If natural rainfall is not expected before the seeds start germinating, Ridomil®2E should be incorporated mechanically before planting or moved into the seed zone after planting with an irrigation system. The following restrictions and limitations are included on the proposed label:

*Do not use Ridomil®2E for disease control in greenhouse crops.
*Do not dip plants in solutions containing Ridomil®2E, or crop injury may result.
*Do not apply under windy conditions.
*Avoid spray overlap as crop injury may result.

Ridomil/Bravo®81W (Cole Crops: Broccoli, Brussels Sprouts, Cabbage, Cauliflower):

Ridomil/Bravo®81W is to be applied as a foliar application in sufficient water to obtain adequate coverage of foliage. Gallonage needed will vary with crop and amount of plant growth. Apply 1.5-2.0 lbs./A (0.14/1.08 lbs. ai/A to 0.18/1.44 lbs. ai/A metalaxyl/chlorothalonil, respectively) in a minimum of 20 gal/A for dilute sprays and 5 gal/A for concentrated ground sprays. Begin when conditions are favorable for disease, but before infection and continue at 14-day intervals until the threat of disease is over. The following restrictions and limitations are included on the proposed label:

*Do not apply within 7 days of harvest, or possible illegal residues may result.
*To minimize the potential for resistance, do not make more than 4 applications of Ridomil/Bravo®81W per crop.
*Do not apply under windy conditions.
*Avoid spray overlap as crop injury may result.

The current registered label for Ridomil/Bravo®81W includes directions for use on broccoli, cabbage, and cauliflower. The proposed label for Brussels sprouts includes all previous restrictions and follows the previous use pattern for Ridomil/Bravo®81W.

No chlorothalonil residue data was submitted in support of the Ridomil/Bravo®81W amendment. Based on the current tolerance for chlorothalonil in or on broccoli, cabbage, cauliflower, and Brussels sprouts of 5.0 ppm, CBTS would be able to conclude that the existing chlorothalonil tolerances are adequate for the proposed use.

Nature of the Residue:

Plant metabolism studies were not submitted with this petition. The Reregistration Standard, Residue Chemistry Chapter indicates the metabolism of metalaxyl in plants is adequately understood. The residues of concern are metalaxyl and its metabolites containing the 2,6-dimethylaniline moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)-alanine methyl ester.

The nature of chlorothalonil residues in plants is not adequately understood (FRSTR, 2/19/88). CBTS notes that additional metabolism studies are required. However, for the purpose of this label amendment which includes chlorothalonil in the metalaxyl formulation, CBTS considers chlorothalonil and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile as the residues of concern.

Animal metabolism data were not submitted with this petition. Since there are no animal feed items involved with this petition, the nature of the secondary residues in animals is not relevant.

Analytical Method-Enforcement:

The Registration Standard Update, Product Chemistry Chapter (4/92) indicates that the Ciba-Geigy analytical method AG-395 adequately recovers metalaxyl residues of concern from plant tissues and has undergone successful Agency validation (PP#3F2978, P. Jung memo of 7/9/84 and PP#8F3617/8H554, F. Griffith memo of 11/28/88). Method AG-395 is a modification of Method I in PAM II. In addition, a multiresidue method is available for metalaxyl in PAM I (PESTDATA, FDA, 11/90). CBTS concludes that adequate methodologies are available for enforcement of the proposed tolerance of metalaxyl on Brassica (cole) leafy vegetables.

Analytical Method-Data Collection:

Mustard greens samples were analyzed with a modification of Ciba-Geigy method AG-395. The method determines total residues of metalaxyl and its metabolites containing the 2,6-DMA moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)-alanine methyl ester as 2,6-DMA by gas chromatography. Results are expressed as metalaxyl equivalents with a limit of detection of 0.05 ppm.

Control samples from the field trials were fortified with metalaxyl at 0.05, 0.10, 0.20, 0.50, 1.0, 10.0, and 20.0 ppm. The petitioner reported that all non-fortified control samples were at <0.05 ppm metalaxyl equivalents, and recoveries from

fortified samples ranged from 76%-99%. Fortification levels and method recoveries presented are adequate.

Storage Stability:

The petitioner has referenced storage stability studies for various raw agricultural commodities (MRID#s 401066-01, 405348-02), including lettuce and cabbage. No data is available for mustard greens, therefore, CBTS will consider the referenced studies.

The Registration Standard requested storage stability data for lettuce (memo, R. Perfetti, 1/15/91). In response to this request, the petitioner referenced a storage stability study (MRID# 401066-01) which was subsequently reviewed in conjunction with PP#0F3893 (memo, R. Lascola, 12/18/91). Lettuce and cabbage samples were fortified with 1.0 ppm each of metalaxyl and 5 regulated metabolites, stored at -15°C, and analyzed for total metalaxyl residues at 0, 6, and 12 months. The parent and 4 of the 5 metabolites were stable up to 12 months. Residues (ppm corrected for procedural recoveries) of metalaxyl and metabolites CGA-62826, CGA-67869, CGA-107955, and CGA-37734 ranged from 0.93-1.3 ppm in lettuce and cabbage. Residues of CGA-94689 at 0, 6, and 12 months were 0.99 ppm, 0.72 ppm, and 0.84 ppm in lettuce; and 0.99 ppm, 0.74 ppm, and 0.74 ppm in cabbage. This storage stability study indicates a decline in metabolite CGA-94689.

Metabolism studies indicate that CGA-94689 accounts for approximately 24.1% of the total identified residues in lettuce at a 7-day preharvest interval (Registration Standard, 6/17/87; PP#0F3893, memo, R. Lascola, 12/18/91). A decline of approximately 30% in CGA-94689 over 12 months (as per the cabbage study) would correspond to apparent residues levels 7% lower than at harvest. CBTS concludes that the lettuce and cabbage storage stability studies indicate some loss of storage and a correction factor of 7% should be applied to results from the mustard greens field trials.

Magnitude of Residue-Field Trials: (MRID No. 421598-01)

Mustard greens field trials were conducted in AZ, CA, FL, GA, MI, TN, and TX. This distribution includes all of the states suggested in the overview of Residue Chemistry Guidelines (memo, R. Schmitt, 10/89) and represents 63% of the domestic mustard greens production (1982 Census of Agriculture, vol. 1, part 51). CBTS concludes the geographical representation is adequate.

Mustard greens were treated with one preplant, broadcast, incorporated application of Ridomil®2E (2.0 lbs ai/A) and four foliar sprays of Ridomil/Bravo®81W (0.18/1.44 lbs./A for each

spray). These applications represent the maximum rate as indicated on the proposed label. Three fields were also treated at 2x the proposed rate. Mustard greens were grown to maturity then harvested at 7 days after the last foliar treatment. Two field trials were harvested the same day as the last application (0-day PHI). Samples were collected and shipped frozen to Ciba-Geigy for analysis, stored frozen (-20°C) from 2 to 11 months, then prepared according to PAM I, Section 141 and Ciba-Geigy SOP 7.20, Revision 1. Sample extracts were stored frozen until residue analysis (1 to 15 days). Metalaxyl residues in or on mustard greens were determined by method AG-395 and reported as metalaxyl equivalents corrected for the method recovery. Levels of chlorothalonil in or on mustard greens were not determined.

Table 1. Metalaxyl residues determined as DMA in mustard greens.

State	Application Rate[a]	PHI (days)	Metalaxyl Equivalents (ppm)[b]
CA	Control	--	<0.05,<0.05[c]
	1x	7	3.1
	1x	7	2.3
	2x	7	14, 15[c]
FL	Control	--	<0.05
	1x	0	8.7
	1x	0	5.0
	Control	--	<0.05
	1x	7	1.6
	1x	7	1.4
MI	Control	--	<0.05
	1x	7	3.1
	1x	7	2.4
	2x	7	4.2
TN	Control	--	<0.05
	1x	7	1.3
	1x	7	1.8
TX	Control	--	<0.05
	1x	7	1.4
	1x	7	0.8
	2x	7	2.5

GA	Control	--	<0.05
	1x	7	4.3
	1x	7	4.4
AZ	Control	--	<0.05
	1x	7	1.5
	1x	7	1.3

[a]1x: 2.0 lbs. metalaxyl/A preplant, broadcast, incorporated treatment at planting plus 0.18 lb./1.44 lbs. metalaxyl/chlorothalonil per acre applied four times as a post foliar spray application.
2x: 4.0 lbs. metalaxyl/A preplant, broadcast, incorporated treatment at planting plus 0.36 lbs./2.88 lbs. metalaxyl/chlorothalonil per acre applied four times as a post foliar spray application.
[b]Results are corrected for procedural recoveries <100%; results are not corrected for control values.
[c]*Samples were reextracted and reanalyzed to confirm result.*

Residue data was reported as corrected for the method recovery. The uncorrected residue levels and chromatogram data were not reported, therefore, the method of calculation from the uncorrected to the corrected values cannot be determined. CBTS requires enough data to determine how corrected values were obtained. Uncorrected residue data (ppm of metalaxyl equivalents) or chromatogram data (peak heights, peak areas, etc.) should be submitted for mustard greens.

The maximum residue for mustard greens treated via 1x the proposed uses, 7-day preharvest interval, was 4.4 ppm from the Georgia field trial. Storage stability studies on lettuce and cabbage indicate a probable loss in storage (see Storage Stability discussion). The maximum residue as corrected for loss in storage is 4.7 ppm metalaxyl equivalents.

A tolerance exists for the crop grouping at 0.1 ppm, except broccoli, cabbage, and cauliflower. A tolerance for broccoli, cabbage, and cauliflower has been set at 2.0 ppm (40 CFR §180.408). The 40 CFR §180.34(f)(5) sets guidelines for establishing a group tolerance: *"If the maximum residues (tolerances) for the representative crops vary by more than a factor of five from the maximum value observed for any crop in the group, a group tolerance will ordinarily not be established."* The representative crops for this grouping are broccoli, cabbage, and mustard greens. CBTS will briefly discuss the available residue data for the two additional representative crops, broccoli and cabbage, as well as for cauliflower (PP#3F2955, memo, F.Boyd, 1/9/84).

The broccoli, cabbage, and cauliflower tolerance represents a similar use pattern as is proposed for mustard greens and Brussels sprouts. Broccoli, cabbage, and cauliflower were

treated with one preplant, broadcast application of Ridomil®2E (2.0 lbs. ai/A), followed by five foliar applications of Ridomil®MZ (0.2 lbs. metalaxyl/A). Results are summarized in Table 2.

Table 2. Maximum metalaxyl residues (ppm) in or on broccoli, cabbage, and cauliflower.

Crop	State	Application type	Application rate (lbs. ai/A)	PHI (days)	Total residues[1]
Broccoli	CA	Soil Broadcast	2.0	73	1.57
	CA	Soil + Foliar	3.0	7	1.21
	CA	Soil + Foliar	3.0	14	1.14
Cabbage	TX	Soil Broadcast	2.0	108	0.15
	CA	Soil + Foliar	3.0	7	0.42
	CA	Soil + Foliar	3.0	14	0.49
Cauliflower	CA	Soil Broadcast	2.0	87	0.57
	CA	Soil + Foliar	3.2	7	0.81
	CA	Soil + Foliar	3.2	14	0.61

[1]Results are corrected for procedural recoveries.

The maximum residues as a result of the soil plus foliar applications were 1.21 ppm for broccoli, 0.49 ppm for cabbage, and 0.81 ppm for cauliflower. Samples were stored frozen for eight to twelve months. After correcting for loss in storage, maximum residues were 1.30 ppm for broccoli, 0.53 ppm for cabbage, and 0.87 ppm for cauliflower. Therefore, tolerances of 1.0 ppm for cabbage and cauliflower, and 2.0 for broccoli would be appropriate.

Ciba-Geigy has proposed a tolerance for the Brassica (cole) crop grouping of 5.0 ppm. Since mustard greens and cabbage maximum residues vary by more than a factor of 5, CBTS cannot recommend in favor of a crop group tolerance for metalaxyl on Brassica (cole) crops. However, a tolerance of 5.0 ppm of metalaxyl on mustard greens would be appropriate provided that CBTS accepts the petitioner's method of correction for the residue data. In addition, there is no established tolerance for chlorothalonil in or on mustard greens. If the petitioner wishes to register Ridomil/Bravo®81W for use on mustard greens, a tolerance will need to be established for chlorothalonil in or on mustard greens.

The current tolerance of 0.1 ppm for the Brassica (cole) leafy vegetables crop group includes Brussels sprouts and exists as a result of seed treatment rather than foliar treatment (PP#3F2827, memo, 11/2/83, P. Errico). Therefore, a tolerance for Brussels sprouts independent of the crop group tolerance at 0.1 ppm should be proposed. If the residue data for a foliar use of metalaxyl on broccoli is translated to Brussels sprouts, a tolerance of 2.0 ppm appears to be appropriate.

Meat, Milk, Poultry, and Eggs:

This petition does not include livestock feed items, therefore an increase in the secondary residues of metalaxyl or chlorothalonil in meat, milk, poultry, and eggs is not expected.

Other Considerations:

There are Codex limits for metalaxyl per se on broccoli, cabbages (head), and cauliflower at 0.5 ppm; and Brussels sprouts at 0.2 ppm. There are no Canadian or Mexican tolerances. The Codex residue of concern is metalaxyl per se. If the U.S. tolerance expression were to be harmonized with the Codex expression, only the parent would be regulated. The metalaxyl Registration Standard (6/87) discusses two metabolism studies on lettuce. The parent accounts for approximately 24%-32% of the total radioactive residue[1]. A tolerance of 0.5 ppm-0.7 ppm (metalaxyl per se) rather than the existing tolerance of 2.0 ppm (metalaxyl and metabolites) may be appropriate. A validated analytical method for metalaxyl per se would be needed. Due to the difference in residues regulated and the difference in residue levels between Codex and U.S. data, compatibility is not possible at this time.

[1]Study 1: 45.2% of total radioactive residue was identified, 14.4% was parent compound; Study 2: 76% of total radioactive residue was identified; 18.6% was parent compound.

Attachment: International Residue Limit Status Sheet.

cc:RF,MetalaxylSF,ChlorothalonilSF,Circ.,PP#2F4072,M.Peters,TOX.
RDI:SecHead:RSQuick:1/13/93:BrSrScientist:RALoranger:1/13/93.
H7509C:MHP:mhp:CM#2:Rm804S:703/305-6380:1/15/93.

F. Kuez
8/27/92

Attachment: Page 1 of 1

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)
Broccoli	0.5
Brussels sprouts	0.2
Cabbages, head	0.5
Cauliflower	0.5

PROPOSED U.S. TOLERANCES:

Petition No. 2F4072

DEB Reviewer M. Peters

Residue: Metalaxyl, its residues containing the 2,6-dimethyl-aniline moiety and N-(2-hydroxymethyl-6-methyl phenyl)-N-(methoxyacetyl) alanine methyl ester.

Crop(s)	Limit (mg/kg)
Brassica (cole) crop group	5.0 ppm

CANADIAN LIMITS:

[✓] No Canadian Limit (on Brassica)

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

[✓] No Mexican Limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES

Form Revised 1989