57

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

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

DEC 18 1991

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Subject: PP#0F3893: Metalaxyl (**Ridomil 2E, 5G**) in/on Leafy Vegetables (Excluding Brassica, Excluding Spinach). Amendment of 9/9/91. CBTS# 8898. MRID# 420211-01. DP Barcode# D171050.

From: Robert Lascola, Chemist
Chemistry Branch I - Tolerance Support
Tolerance Petition Section III
Health Effects Division (H7509C)

Through: P. V. Errico, Section Head
Chemistry Branch I - Tolerance Support
Tolerance Petition Section III
Health Effects Division (H7509C)

To: Ben Chambliss/Susan Lewis, PM-21
Herbicide-Fungicide Branch
Registration Division (H7505C)

CIBA-GEIGY has submitted its response, including a revised Section B, to the deficiencies outlined in S. Bacchus' memo of 6/21/91 concerning the proposed establishment of a tolerance 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-methylphenyl)-N-(methoxyacetyl)-alanine methyl ester, each expressed as metalaxyl, *in/on leafy vegetables (excluding Brassica and spinach) at 5 ppm.*

Tolerances for the combined residues of metalaxyl and its metabolites have previously been established under 40 CFR §180.408(a-c), §185.4000(a-b), and §186.4000(a-b). There are also several pending tolerances for metalaxyl. Metalaxyl is a List A chemical.

Conclusions

1. The petitioner has adequately delineated the dilution volumes for the various applications of **Ridomil 2E and 5G** (Deficiency 2b of S. Bacchus' 6/21/91 memo).

2. The petitioner has adequately described the details of the chromatographic procedures in modified analytical method AG-395. The petitioner has also adequately discussed the apparent residue levels in some control samples (Deficiency 3c of S. Bacchus' 6/21/91

memo).

3. The referenced storage stability study shows that metalaxyl residues in frozen lettuce are not stable over a 12-month storage interval. However, the data, if extrapolated to 15 months, show a limited decline (correction factor = 11.25%). Therefore, the storage stability data are adequate for this petition (Deficiency 4 of S. Bacchus' 6/21/91 memo).

4. Application of the correction factor arising from the storage stability study indicates that residue levels for head lettuce, leaf lettuce, and celery are still within the proposed 5 ppm crop group tolerance.

5a. CBTS concludes that the revised Section B, which no longer indicates foliar application of **Ridomil** alone, is consistent with the use patterns exhibited in the residue trials. However, CBTS finds that the label still contains deficiencies. Specifically, the label currently implies that application of mancozeb to leafy vegetables is legal, whereas there is only one leafy vegetable crop, celery, for which there is a tolerance (5 ppm). In addition, a Special Review has been initiated for mancozeb and revocation of all tolerances (including celery) has been proposed. Since there are no tolerances for mancozeb on all other non-Brassica leafy vegetables besides celery, the petitioner must submit a revised Section B which does not include foliar application of the mancozeb/metalaxyl mixture on those crops. Furthermore, if the Agency elects to revoke the mancozeb tolerance on celery, the petitioner will have to remove foliar application of the mancozeb/metalaxyl mixture on that commodity as well. (Deficiency 5b of S. Bacchus' 6/21/91 memo.)

5b. CBTS concludes that the late harvest and high temperatures for trial 02-FR-006-89 do not represent normal conditions for growing celery, that the celery grown under these conditions would be unusable, and that any field trial results obtained under those conditions would be invalid. Therefore, the residue values for use of 1x the label rate of **Ridomil 5G** on celery range from 0.19-2.1 ppm. CBTS further concludes that the residue data support the proposed crop group tolerance of 5 ppm for metalaxyl on leafy vegetables (except Brassica, except spinach). (Deficiency 5b of S. Bacchus' 6/21/91 memo.)

Recommendation

CBTS recommends **against** the proposed crop group tolerance of 5 ppm for metalaxyl on leafy vegetables (except Brassica, except spinach) for the reason delineated in Conclusion 5a.

Detailed Considerations

Each of the deficiencies outlined in our previous memo will be repeated, followed by the

petitioner's response and our comments.

- **Deficiency 2b.** A revised Section B stating the amount of solvent or water to be used for the proposed application rates is required.

  Petitioner's Response. The petitioner has submitted a revised Section B for **Ridomil 2E** and **5G** which now calls for application of 1-2 lbs ai/A dissolved in a minimum of 20 gals of water or liquid fertilizer for preplant incorporated or surface applications. For foliar application, the recommended rate of 0.87-1.16 lbs ai/A mancozeb/metalaxyl should be dissolved in a minimum of 20 gals of water. Also, the **Ridomil 2E** labelling specifies application for control of white rust on spinach only. For this use, in addition to the preplant incorporated or surface application described above, 0.125 lb ai of metalaxyl/A of crop should be applied, shanked in 40-50 days after planting or after each cutting.

  CBTS's Response. Although an application volume is not specifically indicated for the white rust control application, it is implied that the same dilution procedures would be used as for the preplant incorporated or surface applications. Therefore, CBTS considers that the dilution procedures have been adequately delineated and that this deficiency is resolved.

- **Deficiency 3c.** Samples of leaf lettuce and celery were analyzed by a modified method AG-395 in which the derivatization step was eliminated. The underivatized DMA shows a retention time of approximately 14.05 min (leaf lettuce, celery). The hydrolysis step is essentially unchanged and recovery of the regulated metabolite has been previously demonstrated (RS, 6/22/87). This method may be adequate to support the petition. However, the petitioner should provide details of the columns, column conditions and instrumentation used. An explanation of the control values which exceed the limit of detection (< 0.05-0.16 ppm) is also required.

  Petitioner's Response. The petitioner has submitted the requested details concerning the instrumentation, columns, and column conditions for the GC-NPD and GC-MS methods used in the modified analytical method AG-395.

  The petitioner suggests four potential reasons for the apparent residues in head lettuce, leaf lettuce, and celery control samples. 1) There are natural plant products which convert to 2,6-dimethylaniline or an isomer with similar chromatographic and mass spectral properties. 2) There was spray drift during the application (considered unlikely by the petitioner). 3) There was cross-contamination during field trials and/or sampling (also considered unlikely by the petitioner). 4) There was "volatility of the applied chemical which would be influenced by weather and/or soil conditions."

  The petitioner further states, "In any event, the apparent residue levels in the controls (0.06-0.16 ppm) are generally much lower than those found in treated samples (average residues 0.84-1.5 ppm) and significantly lower than the established tolerance for head lettuce (5.0 ppm)."

CBTS's Response. CBTS concludes that the petitioner has adequately resolved this deficiency.

- **Deficiency 4.** The Registration Standard has requested storage stability data for lettuce (memo, R. Perfetti, 1/15/91). The registrant should provide CBTS with documentation of the studies in progress to satisfy the RS requirements. If these data indicate that the residues are stable for 3 to 15 month intervals, they can be used to support this tolerance request.

Petitioner's Response. The petitioner notes that the Registration Standard asks that storage information be provided for lettuce residue data submitted under MRID# 0097511. "The missing data relate only to sample storage intervals for lettuce samples used to support current tolerances and, therefore, have no bearing on the newly proposed group tolerances." The petitioner cites MRID# 401066-01, which it claims shows that metalaxyl and five individually fortified metabolites are stable in lettuce for a minimum of 12 months at freezer storage temperature. This study was not reviewed in the 1988 FRSTR. Also cited are a study which shows that field-incurred residues of metalaxyl in potatoes and tobacco are stable for 18 months under freezer storage conditions (MRID# 00071678) and an in-progress study which shows that field-incurred residues of metalaxyl in spinach, peppers, potatoes, and cranberries are stable for at least one year. The latter study will be conducted for up to 38 months and will be completed in mid-1994. "Based on the data currently available, there is no reason to expect that residues of metalaxyl in lettuce, determined as DMA, would not be completely stable under freezer storage conditions for 3-15 months."

CBTS's Response. The referenced study, MRID# 401066-01, contains 12-month storage stability data for 5 commodities including lettuce and cabbage. Samples were injected with 1.0 ppm spikes of metalaxyl and 5 metabolites and were kept in storage at -15 °C. Samples were analyzed for "total" metalaxyl residues at 6-month intervals over a one-year period. Results for lettuce and cabbage are provided below.

Table 1. 12-Month Storage Stability of Metalaxyl in Lettuce and Cabbage.

	Lettuce (ppm)[1]			Cabbage (ppm)[1]		
months	**0**	**6**	**12**	**0**	**6**	**12**
metalaxyl	1.0	1.1	0.98	1.0	0.93	1.1
CGA-62826	1.0	1.0	1.1	1.0	0.94	1.0
CGA-67869	1.0	1.2	1.2	1.0	0.94	0.96
CGA-107955	0.99	1.3	0.95	1.0	1.1	0.95
CGA-37734	0.99	1.0	1.2	1.0	0.97	0.96
CGA-94689	0.99	0.72	0.84	0.99	0.74	0.74

1 - Values represent average of duplicate samples and are converted for procedural recoveries.

The petitioner claims that the apparent decline in residues observed for metabolite CGA-94689 does not mean that that metabolite is unstable in those commodities. They conclude that the decline is due to experimental deviation for three reasons: residues of CGA-94689 show no decline over a 12-month period in strawberries and apples, residues did not decline between the 6th month and 12th month measurements, and there was a "low accountability" of the metabolite by the method (average recovery was 30%).

CBTS concludes that this study shows that metalaxyl residues in frozen lettuce are not stable over a 12-month storage interval. We do not agree with the petitioner's assessment that the decline in residues over a 12-month period for the metabolite CGA-94689 is due to experimental uncertainty. The stability of the chemical in fruits does not necessarily imply the same stability in leafy vegetables. Also, the metabolites CGA-107955 and CGA-37734 were observed to be stable in lettuce notwithstanding the "low accountability" of the method for their detection (47% and 61%, respectively).

However, the decline may be described as a limited decline, meaning that correction factors may be applied to the residue data. As is discussed in the 6/17/87 Registration Standard, in two lettuce metabolism studies CGA-94689 accounted for 24.1% (7-day PHI) and 29.1% (14-day PHI) of the total identified residue.[1] A decline of approximately 30% in CGA-94689 residues over 12 months (as seen in the cabbage study) would thus correspond to apparent residue levels 9% lower than existed at harvest. If we assume that the rate of decline is constant from 12 months to 15 months, we can estimate the correction factor to be (9% x 1.25 =) 11.25%. The impact of this correction on the residue data submitted for this petition and the adequacy of the proposed tolerance will be dicussed below. CBTS concludes that the storage stability data are adequate for this study.

Application of this correction factor to the observed residue values shows that for application of 1x the recommended rate, the maximum residue levels are 4.7 ppm (7 day PHI) or 4.4 ppm (14 day PHI) for head lettuce, 4.2 ppm (5 day PHI) for leaf lettuce, and 2.3 ppm (5 day PHI) for celery (also see the discussion of Deficiency 5b, below). These residues are within the proposed 5 ppm tolerance for the leafy vegetable (except Brassica and spinach) group.

- **Deficiency 5b.** No residue data reflecting the foliar use of the **Ridomil 2E** formulation and the proposed soil and foliar treatment has been submitted. The petitioner should submit field residue data using the **Ridomil 2E** and **5G** formulation at the maximum proposed soil and foliar use rates and the minimum PHI from the major growing areas in the US. If the petitioner wishes to pursue a crop group tolerance, and if one representative crop is excluded, residue data for another similar crop in the group should be substituted. Based on the variability of the residue data submitted thus far, a crop group tolerance may not be appropriate. The petitioners may

---

[1] - Test 1: MRID# 114379. 87.7% of the activity was recovered; 45.2% was identified; 10.9% was CGA-94689. Test 2: MRID# 71608. 76.0% of the activity was identified; 22.1% was CGA-94689.

need to propose alternate tolerances on the individual crops used in the field trials. A final decision will be made when the residue data requested above have been submitted.

Petitioner's Repsonse. The petitioner has responded to this deficiency in two parts. The first part addresses the lack of residue data reflecting the foliar use of **Ridomil 2E**. "As part of CIBA-GEIGY's resistance management program for metalaxyl, foliar applications are not labeled, except in a couple of special situations, for **Ridomil 2E** Fungicide. It is not CIBA-GEIGY's intention to label **Ridomil 2E** alone for foliar application to leafy vegetables. Such a practice would be contrary to our resistance policy. Therefore, additional residue data reflecting foliar applications of **Ridomil 2E** are not justified because **Ridomil 2E** will not be labeled for foliar applications. This plan is reflected in the labels that were submitted with this petition.

"The confusion stems from the inclusion in the Section B of a foliar application of **Ridomil 2E**, rather than **MZ58**. This circumstance stems from an assumption on our part that was incorrect. To alleviate this confusion, a revised Section B is enclosed which more correctly reflects the use pattern utilized in the residue trials." (Emphasis is the petitioner's.)

This revised Section B now calls for foliar application of 0.87-1.16 lbs ai/A of a mancozeb/metalaxyl mixture in a 4.8:1 ratio, whereas the previous label had called for foliar application of metalaxyl alone.

The second part interprets our statement "Based on the variability of the residue data submitted thus far, a crop group tolerance may not be appropriate" as stemming from the statement located in the body of the review, "It would appear that the maximum residues observed in celery, therefore, may even exceed the 10 ppm tolerance established for spinach. The maximum residue (11 ppm) observed for celery cannot be considered an outlier since it is within 3 standard deviations of the mean (3.86 ± 4.17). Therefore, for this proposed use, the requested tolerance for the leafy vegetables crop group cannot be recommended."

CIBA-GEIGY states, "The highest metalaxyl residue observed in celery was from a California trial, 02-FR-006-89, which encountered a series of adverse conditions, including extremely high temperatures that caused significant leaf burn. This circumstance was documented in the Field Procedures section of ABR-89113. For all practical purposes, this field test should be considered invalid owing to extreme weather conditions, which resulted in a celery crop that was undersized and of unmarketable quality. Therefore, excluding the maximum 1X residue (11 ppm) observed in one of four California celery tests, the maximum 1x celery residue was 2.1 ppm, which is within the proposed 5 ppm group tolerance."

CBTS's Response. CBTS concludes that the revised Section B, which no longer indicates foliar application of **Ridomil 2E** alone, is consistent with the use patterns exhibited in the residue trials. However, CBTS finds that the label still contains deficiencies. Specifically, the label currently implies that application of mancozeb to leafy vegetables is legal, whereas there is only one leafy vegetable crop, celery, for which there is a tolerance (5 ppm). In addition, a Special

Review was initiated for mancozeb and the other EBDC fungicides on 7/10/87. The PD 2/3 Preliminary Determination (54 FR 52158, published 12/20/89) proposed cancellation of use of mancozeb on celery and other crops. Cancellation of mancozeb tolerances on all crops was later proposed in 55 FR 20416 (5/16/90). The PD 4 Final Determination will be published 12/91. Since there are no tolerances for mancozeb on all other non-Brassica leafy vegetables besides celery, the petitioner must submit a revised Section B which does not include foliar application of the mancozeb/metalaxyl mixture on those crops. Furthermore, if the Agency finalizes the revocation of all mancozeb tolerances, the petitioner will have to remove foliar application of the mancozeb/metalaxyl mixture on celery as well.

With regards to the residue value from trial 02-FR-006-89, the petitioner has included in the Field Procedures report the average temperatures for January - June of 1989. Temperatures in June averaged 77.0 °F, 2 degrees above normal. Harvest of the crop was in mid-July. CBTS obtained data[2] which showed that the average temperature in Fresno County, where the test was conducted, in July 1989 was 82.4 °F (average high 99.2 °F, maximum 107 °F). According to Considine[3], "Celery plants will tolerate considerable heat after they are established in the field, but during the last month or so preceding harvest, temperatures should average no more than 60 to 70 °F." This is confirmed by a USDA Cooperative Extension specialist[4] who stated (telecon, 12/6/91) that "a few days above 85 degrees will make the celery pithy or spongy and it will have no value". He further explained that it was unusual to grow celery in that region of California, because of the high temperatures, and if celery was grown there, it would normally be harvested by the beginning of June.

CBTS concludes that the late harvest and high temperatures for trial 02-FR-006-89 do not represent normal conditions for growing celery, that the celery grown under these conditions would be unusable, and that any field trial results obtained under those conditions would be invalid. Therefore, the residue values for use of 1x the label rate of **Ridomil 5G** on celery range from 0.19-2.1 ppm. CBTS further concludes that the residue data support the proposed crop group tolerance of 5 ppm for metalaxyl on leafy vegetables (except Brassica, except spinach).

cc: R. Lascola, PP#0F3893, RF, SF, RS (metalaxyl), C. Furlow (PIB/FOD), Circ, R.S. Quick.

RDI: P.V. Errico: 12/17/91; R. Loranger:12/17/91.
H7509C:CBTS/HED:CM#2, Rm803C: R. Lascola/rjl,305-7478:12/12/91
O:Disk1\METALAXY\3893A.TXT

---

[2] - From National Climatic Data Center, (704) 259-0682.

[3] - Considine and Considine, Foods and Food Production Encyclopedia (1982).

[4] - Dr. Vincent Rubatzky, UC-Davis: (916) 752-1247.