



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

JUL 22 1993

MEMORANDUM:

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Metalaxyl, Reregistration. Registrant Ciba-Geigy
Submission on Magnitude of the Residue in Peanuts and
Processed Commodities of Rice, Sunflower, and Pineapple
(MRID Nos. 42498701, 42498702).
CBRS No. 11238. DP Barcode No. D187081.

FROM: John Abbotts, Chemist *John Abbotts*
Special Review Section II
Chemistry Branch II - Reregistration Support
Health Effects Division [H7509C]

THRU: Francis B. Suhre, Section Head *Francis B. Suhre*
Special Review Section II
Chemistry Branch II - Reregistration Support
Health Effects Division [H7509C]

TO: Lois Rossi, Chief
Reregistration Branch
Special Review and Reregistration Division [H7508C]

Attached is a review of residue chemistry data for magnitude of the residue in peanuts and processed commodities of rice, sunflower, and pineapple, submitted by registrant Ciba-Geigy Corporation in support of reregistration and in response to previous reviews. This information was reviewed by Acurex Corporation under supervision of CBRS, HED. The data assessment has undergone secondary review in the branch and has been revised to reflect branch policies. The review reached the following conclusions:

- To support use on peanuts, label amendments for 1% G formulations imposing a PHI of 75 days are required.
- Residue data for rice processed commodities are acceptable.
- Residue data for sunflower seed processed commodities are acceptable, and the registrant's proposed feed additive tolerance for sunflower seed meal is appropriate.
- Storage stability data are required to support residue data on pineapple processed commodities.

If you need additional input please advise.

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CBRS 11238, Metalaxyl Reregistration, p. 2 of 2

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METALAXYL
(Chemical Code 113501)
(CERS No. 11238; DP Barcode D187081)

TASK 3

**Registrant's Response
to Residue Chemistry Data
Requirements**

April 22, 1993

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

Acurex Environmental Corporation
Eastern Regional Operations
4915 Prospectus Drive
P.O. Box 13109
Research Triangle Park, NC 27709

METALAXYL

(Chemical Code 113501)

(CBRS No. 11238; DP Barcode D187081)

REGISTRANTS RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

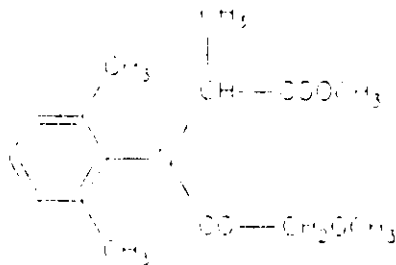
Task-3

BACKGROUND

The Metalaxyl Guidance Document dated 9/88 required residue chemistry data pertaining to processing studies on potatoes, sugar beets, corn, rice, sorghum, cottonseed, pineapples, and sunflower seeds. In response, CIBA-GEIGY Corp. submitted data pertaining to residues in or on peanut commodities and processing studies on potatoes, corn, rice, sorghum, cottonseed, and sunflower seed. These data were reviewed by the Agency (CBRS No. 8043, 6/1/92, L. Cheng). In addition, the registrant submitted a pineapple processing study that was subsequently reviewed by the Agency (CBRS No. 9596, 6/22/92, R. Perfetti). These Agency reviews cited deficiencies that are addressed in the current submission (1991-92; MRIDs 42498701 and -02). The Conclusions and Recommendations stated herein pertain only to the magnitude of the residue in peanuts and processed commodities of rice, sunflower, and pineapple.

The qualitative nature of the residue in plants is adequately understood. The residues of concern are those expressed in the current tolerances as 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-hydroxy methyl-6-methyl)-N-(methoxyacetyl)-alanine methyl ester [40 CFR §180.403(a)-(c), §185.4000(a)-(d), and §186.4000(a)-(d)]. Adequate enforcement methodology exists as Methods I and II in PAM, Vol. II (methods AG-348 and AG-349).

Codex MRLs of 0.05 ppm have been proposed (Step 6) for residues of metalaxyl per se in or on potatoes, cottonseed, and sunflower seed. These MRLs differ from the U.S. tolerances with respect to residue level and the compound(s) regulated. Compatibility of these MRLs with the corresponding U.S. tolerances could not be achieved without a major revision in the U.S. tolerance definition. There are no Codex MRLs proposed or established for metalaxyl residues in or on cereal grains or peanuts.



Metalaxyl

CONCLUSIONS

1. The registrant's explanations of apparent residues in control samples of sunflower commodities are adequate. Available residue data support the existing tolerance for combined residues of metalaxyl of 0.1 ppm in or on sunflower seed and sunflower, forage.
2. The registrant's explanations of apparent residues in control samples of peanut commodities have previously been reviewed and accepted (CBRS 10743, 10744, 11/24/92, L. Cheng).
3. The label amendments for the 1% G formulation (EPA Reg. Nos. 100-664 and 100-713) have previously been reviewed, and CBRS concluded that a PHI of 75 days must be imposed (CBRS 10743, 10744, 11/24/92, L. Cheng).
4. The registrant provided calculations showing the 1x treatment rate is equivalent to 0.0313 lbs ai/A (0.5 oz ai/100 lbs of seed; at 100 lbs of seed/A). Broadcast preemergence soil applications were made at 2.0 and 6.0 lbs ai/A, representing exaggerated rates of 64x and 192x. The submitted calculations are adequate.
5. Because combined residues in rice bran at exaggerated rates up to 162x are less than the tolerance for grain crops of 0.1 ppm, a food additive tolerance for bran is not required. Residue data for rice processed commodities are acceptable.
6. The registrant's proposal for a feed additive tolerance of 0.2 ppm in sunflower seed meal is appropriate. Residue data for sunflower seed processed commodities are acceptable.
7. No storage stability data on pineapple fruit or forage were submitted. The registrant has proposed translating to other crops, data from existing storage stability studies on potatoes, tobacco, strawberry, apple, cabbage, and lettuce as well as an ongoing 3-year storage stability study on cranberries, peppers, potatoes, and spinach. If

metalaxyl residues of concern are stable in all crops tested it is reasonable to allow translation of these data to support the storage stability of other crops for which tolerances are established. However, if all residues of concern are not stable under the conditions and for the intervals incurred in obtaining data in support of tolerances, then CBRS may recommend further storage stability studies (CBRS 8723, 1/22/92, W. Smith).

8. Pending the storage stability data required to resolve Conclusion 7, residue data on pineapple processed commodities are acceptable, and a feed additive tolerance of 0.5 ppm is appropriate for pineapple bran.

RECOMMENDATIONS

Label amendments for use on peanuts are required to satisfy Conclusion 3.

Registrant's proposed food additive tolerance of 0.2 ppm for sunflower seed meal is appropriate (Conclusion 6). Contingent upon the availability of storage stability data to validate the pineapple processing study (Conclusion 7), registrant's proposed feed additive tolerance of 0.5 ppm for pineapple bran is appropriate.

DETAILED CONSIDERATIONS

In the current submission (1991-92; MRIDs 42498701 and -02), the registrant has provided responses to deficiencies listed in two recent Agency reviews (CBRS 8043, 6/1/92, L. Cheng, and CBRS 9596, 6/22/92, R. Perfetti). The following DETAILED CONSIDERATIONS are formatted so that numbering follows that of the deficiencies identified in the applicable Agency review.

Responses to CBRS No. 8043, 6/1/92, L. Cheng

§171-4 (c and d). Residue Analytical Methods.

CBRS Deficiency no. 1.

Method AG-395 adequately recovered metalaxyl from fortified samples. However, apparent residues in or on untreated sunflower seeds and control samples of all processed commodities were above the stated 0.05 ppm detection limit. Moreover, apparent residues were greater than the 0.1 ppm tolerance level in four of eight control seed samples reported and also in control seed meal. High apparent residues were observed in untreated peanut hulls, vines, and hay also. The registrant needs to explain these findings.

Registrant's Response to Deficiency no. 1

CIBA-GEIGY (MRIDs 42498701 and -02) reported on possible sources of contamination of control samples as follows: (i) spray drift during application; (ii) cross contamination during the field trial or sampling; (iii) extraction of natural products from plants by analysis procedure; and (iv) volatility of the applied chemical; which could be influenced by weather or soil conditions. The registrant reported that upon re-examination of the retained sunflower seeds from this study the seeds were found to be contaminated with an "an unusual amount of foliar crop debris," indicating possible contamination of the seeds with forage; the forage control contained apparent residues of 0.46 ppm. Therefore, the registrant attempted to remove the "debris" and reanalyzed the seed control samples (two samples). The reported results are summarized in Table 1 below.

Table 1. Reanalysis of sunflower seed and forage control samples for metalaxyl residues.

Sample Type and Number	Residues Found (PPM)		
	Original Analysis	Reanalysis with debris	Reanalysis cleaned
Seed			
001003A	0.14, 0.18	0.083	0.053
001003B	Not analyzed	0.084	0.052
Forage			
001003A	NP*	NP	0.21, 0.16
001003B	NP	NP	0.46

*NP=not provided; data not provided by registrant in this submission.

In its cover letter to the present submission (MRID 42498700), registrant Ciba-Geigy indicated it would have no objection to establishing a tolerance on sunflower, forage at combined residues of metalaxyl of 2.0 ppm. However, the Residue Chemistry Second Round Review (6/22/87) concluded that available residue data supported the established tolerance of 0.1 ppm in or on sunflower seed and sunflower, forage. The higher residues on control samples are considered anomalous, and the existing tolerances are adequate.

Regarding peanut vines and hay, the registrant's explanation of high residues on control samples has previously been reviewed and accepted; peanut residue data in MRID 41870306 were considered acceptable (CBRS 10743, 10744, 11/24/92, L. Cheng).

CBRS Conclusion

The registrant's explanations of apparent residues in control samples of sunflower commodities are adequate. Available residue data support the existing tolerance for combined residues of metalaxyl of 0.1 ppm in or on sunflower seed and sunflower, forage.

The registrant's explanations of apparent residues in control samples of peanut commodities have previously been reviewed and accepted (CBRS 10743, 10744, 11/24/92, L. Cheng).

§171-4 (k). Magnitude of the Residue in Plants.

CBRS Deficiency no. 2.

Peanuts.

- 2a. The peanut field trial data indicate that tolerance-exceeding residues can result in or on peanut nutmeats from at-pegging applications of a G formulation at 1 lb ai/A (the maximum rate for this registrant's 1% G MAI formulation). The registrant stated that these data were submitted in support of the 5% G label (EPA Reg No. 100-628), on which a maximum rate of 0.5 lb ai/A is specified at pegging.
- 2b. If the registrant does not intend to support the 1% G formulation (EPA Reg. No. 100-664), they should cancel this registration or amend this label to specify a maximum rate of 0.5 lb ai/13,000 linear feet. Otherwise they must propose a revised tolerance that is supported by adequate residue data. In addition, an explanation of the high apparent residues in control samples of hay (up to 4.5 ppm), hulls (0.63 ppm), and vines (2.4 ppm) is required, in order for these data to be found acceptable.
- 2c. Residue data are adequate to support reregistration of metalaxyl on peanuts, provided the maximum use rate (at-pegging) for both the 1% and 5% G formulations is 0.5 lb ai/A or 0.5 lb ai/13,000 linear feet with 40-inch row spacing. Since the residue data were generated at PHIs of 65-92 days, the current PHI (45 days) must also be amended.

Registrant's Response to Deficiency no. 2.

In the present submission (MRID 42498701), CIBA-GEIGY stated that the 1% G label will be amended to specify 0.5 lb ai/14,520 linear feet at early pegging with 36-inch row spacing. These label amendments have previously been reviewed, with no MRID No. assigned (CBRS 10743, 10744, 11/24/92, L. Cheng). CBRS concluded that in order that the established tolerance for combined metalaxyl residues in peanuts of 0.2 ppm not be exceeded, a PHI of 75 days must be imposed on 1% G formulations, Ridomil PC[®] 11G (EPA Reg. No. 100-664) and Ridomil PC (EPA Reg. No. 100-713).

CBRS Conclusion

The label amendments for the 1% G formulation (EPA Reg. Nos. 100-664 and 100-713) have previously been reviewed, and CBRS concluded that a PHI of 75 days must be imposed (CBRS 10743, 10744, 11/24/92, L. Cheng).

§171-4 (l). Magnitude of the Residue: Processed Food/Feed.

CBRS Deficiency no. 5.

Rice.

- 5a. The available data on rice are insufficient to determine the potential for concentration of residues during processing. The data indicate that residues concentrated in bran processed from grain with residues below the validated detection limit. The raw data needed to determine the actual residues in or on grain were not provided. Therefore, a concentration factor could not be calculated.
- 5b. In the submission on rice, the registrant estimated the exaggerated rates of the broadcast preemergence treatments by comparing those rates with the amount of active ingredient applied to seed for planting one acre and arrived at overestimated factors of 64 and 192x. The registrant must explain the calculations used to arrive at these estimates.

The previous review (CBRS 8043, 6/1/92, L. Cheng) noted that in cases when RAC samples with no detectable residues yield processed samples with detectable residue, the Agency may estimate residue levels from chromatograms where the response is below the validated limit of detection but indicative of a measurable value.

Registrant's Response to Deficiency no. 5.

CIBA-GEIGY (MRID 42498701) responded by providing the chromatograms requested; they also provided tabulated (actual and apparent) residues found in rice (RAC) and rice bran for the control (untreated), and 1x, 64x and 192x treatments. The submitted summary table is presented below as Table 2.

Table 2. Total residues (in metalaxyl equivalents) in rice and rice bran from control plants, and plants treated at 1x, 64x, and 192x.

Rate	Residue (PPM)		Concentration
	Rice (RAC)	Rice bran	
control*	0.0088	0.043	4.9
1x	0.0103	0.048	4.7
64x	0.0088	0.048	5.5
192x	0.0118	0.054	4.6

*Corrected for concurrent method recoveries.

In response to conclusion 5b, the registrant provided calculations showing the 1x treatment rate is equivalent to 0.0313 lbs ai/A (0.5 oz ai/100 lbs of seed; at 100 lbs of seed/A). Broadcast preemergence soil applications were made at 2.0 and 6.0 lbs ai/A, representing exaggerated rates of 64x and 192x.

The registrant noted that residue levels in the controls (RAC and bran) resulted in a concentration factor of 4.9, and the average concentration factor (1x, 64x, 192x) for the treated samples was the same level (4.9). Because combined residues in rice bran at exaggerated rates up to 162x are less than the tolerance for grain crops of 0.1 ppm, a food additive tolerance for bran is not required.

CBRS Conclusion

The submitted rate calculations are adequate.

No food additive tolerance for rice bran is required. Residue data for rice processed commodities are acceptable.

CBRS Deficiency no. 6.

Sunflower seeds.

6. The sunflower seed processing study indicated that residues concentrated up to 1.5x in seed meal. The registrant must propose a feed additive tolerance for residues in sunflower seed meal. The data indicate that a level of 0.2 ppm would be appropriate. Residues did not concentrate in hulls, crude oil, refined oil, or soapstock.

Registrant's Response to Deficiency no. 6.

In its cover letter (MRID 42498700), registrant CIBA-GEIGY proposed a feed additive tolerance of 0.2 ppm for sunflower meal.

CBRS Conclusion

The registrant's proposal for a feed additive tolerance of 0.2 ppm in sunflower meal is appropriate. Residue data for sunflower seed processed commodities are acceptable.

Response to CBRS No. 9596, 6/22/92, R. Perfetti

CBRS Deficiency no. 2.

§171-4 (e). Storage Stability Data

2. No storage stability data were reported in the current submission. Requirements remain outstanding for data depicting the stability of metalaxyl residues of concern in or on pineapple fruit and forage stored under similar conditions and for similar intervals as residue samples for which data have been submitted. Because storage intervals for processed samples were relatively brief (< 3 months), storage stability data will not be required for pineapple processed fractions, unless the required stability data for pineapples indicates that residues decline in the first 3 months of frozen storage.

Registrant's Response to Deficiency no. 2.

CIBA-GEIGY (MRID 42498701) resubmitted a summary of potato, tobacco, strawberry, apple, cabbage, and lettuce storage stability data as well as a brief description of an ongoing 3-year storage stability study on cranberries, peppers, potatoes, and spinach. The registrant stated that: (i) residues of the parent are stable in fortified potatoes and tobacco for 12 months, and in weathered potatoes and tobacco for 18 months; (ii) parent and 5 metabolites are stable in fortified strawberries, apples, cabbage, lettuce, and potatoes for up to 12 months; and (iii) interim one year results show no decline in total residues in cranberries, peppers, potatoes, and spinach. From these data the registrant concluded that (assuming complete stability of the total metalaxyl residues in all crops in the ongoing study) that these (3) studies would provide an adequate data base which could be translated to other crops.

CBRS Conclusion

This summary was reviewed previously (CBRS 8723, 1/22/92, W. Smith). CBRS reiterates, we cannot officially concur with the registrant's conclusion prior to completion of studies and review of all data. We do agree with the registrant that if metalaxyl residues of concern are stable in all crops tested it is reasonable to allow translation of these data to support the storage stability of other crops for which tolerances are established. However, if all residues of concern are not stable under the conditions and for the intervals incurred in obtaining data in support of tolerances, then CBRS may recommend further storage stability studies.

CBRS Deficiency no. 3.

§171-4 (l). Magnitude of the Residue: Processed Food/Feed.

Pineapples.

3. The available data on pineapples are insufficient to determine the potential for concentration of residues during processing. The data indicate that metalaxyl residues concentrated in dried pineapple bran processed from pineapples with residues below the validated detection limit. The raw data needed to determine the actual residues in or on bran were not provided. Therefore, a concentration factor could not be calculated. The registrant must submit full-sized copies of the chromatograms for the pineapple fruit and dried bran samples from the 7x treatment, along with raw data showing estimates for residues below the validated detection limit.

Registrant's Response to Deficiency no. 3.

CIBA-GEIGY (MRID 42498701) provided the requested raw data; they also provided tabulated residues found in pineapple (RAC) and dried bran. The submitted summary table is presented below as Table 3. The registrant stated that a feed additive tolerance of 0.5 ppm should be appropriate.

In addition, the registrant stated that they were informed by Mr. James Tompkins (Registration Support Branch) that tolerances required as a result of reregistration will not be subject to the filing of a petition by the registrant, but that the Agency will at some point in the future propose and establish tolerances based on the available data.

Table 3. Total residues (in metalaxyl equivalents) in pineapple and pineapple bran from plants treated at 7x.

Commodity (sample)	Residue (PPM)		Method Recovery
	Uncorrected	Corrected	
Dried bran	0.069	0.108	64.13
Pineapple (a)	0.017	0.023	75.28
Pineapple (b)	0.018	0.024	75.28
Concentration	3.9	4.6	--

*Corrected for concurrent method recoveries.

CBRs Conclusion

Pending adequate storage stability data, residue data on pineapple processed commodities are acceptable, and a feed additive tolerance of 0.5 ppm is appropriate for pineapple bran.

References:

Citations for the MRID documents and Agency correspondence referred to in this review are presented below. Submissions reviewed in this document are indicated in shaded type.

- 42498701 Ross, J. (1992) Response to EPA Review of Metalaxyl on Cereal Grains, Soybeans, Potatoes, Peanuts, Cottonseed, Sunflower Seed, and Pineapples: Lab Project Number: ABR-92054. Unpublished study prepared by Ciba-Geigy Corp. 81 p.
- 42498702 Smith, J. (1992) Metalaxyl: Amendment to Magnitude of Residue in Processed Food/Feed Commodities of Sunflowers Following Seed Treatment with Apron 25W: Lab Project Number: ABR-90105: 409222. Unpublished study prepared by Ciba-Geigy Corp. 21 p.

Agency Memoranda

CBRS No.: 8043
Subject : Metalaxyl. Ciba-Geigy Response to Guidance Document (FRSTR) Dated 9/88.
To: L. Rossi
From: L. Cheng
Dated: 6/1/92
MRID(s): 418703-01 through -07

CBRS No.: 8723
Subject : Metalaxyl Reregistration: Ciba-Geigy Corporation: Request for concurrence with Storage Stability Protocol
To: C. Peterson
From: W. Smith
Dated: 1/22/92
MRID(s): None

CBRS No.: 9596
Subject : Ciba-Geigy Corp.: Response to the Metalaxyl Reregistration Standard: Residue and Processing Data
To: W. Burnam
From: R. Perfetti
Dated: 6/22/92
MRID(s): 42233501

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CBRS No.: 10743, 10744
Subject : Metalaxyl. Label Amendments for Peanuts.
To: B. Chambliss
From: L. Cheng
Dated: 11/24/92
MRID(s): None