Metalaxyl S.F.

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

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Mefenoxam: Replacement of Metalaxyl Technical with Mefenoxam Technical; Review of Bridging Data, D223261. CBTS No. 16909. PRIORITY 6. MRID 438003-00,-01,-22 and -23. 438898-01,-02,-03,-21 438969-01,-02,-03,-04,-05. TOX 375AA, ID #:000100-TOR PRAT CASE #: 039771

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Ciba-Geigy proposes registration of mefenoxam technical (CGA 329351, chemical number 113502) with the intent of replacing metalaxyl technical (CGA 48988, chemical 113501) for manufacturing of end-use products. Mefenoxam, the R-enantiomer of metalaxyl, has been found to be more effective in disease control than metalaxyl technical (the combination of R and S enantiomers) or the S-enantiomer. Due to its increased fungicidal activity, the proposed use rate of mefenoxam is one half the rate used for metalaxyl. Tolerances to support registered metalaxyl uses are established for numerous plant and animal commodities [40 CFR 180.408 (a) and (c), 185.4000 (a), and 186.4000 (a)].

This submission contains proposed labels; product chemistry data; method validation for plants; residue data for lettuce, tomatoes, potatoes, tobacco and cabbage; and a confidential statement of formula in support of the proposed registration of mefenoxam in place of metalaxyl in/on the RACs on which metalaxyl is currently used.

Metalaxyl is a list A chemical. (The product chemistry and residue chemistry chapters for the metalaxyl RED have been completed by CBRS. See 6/16/94 memo of Sue Hummel, D197037).

CONCLUSIONS

1a. All product chemistry data requirements for mefenoxam have been adequately met. Reviews of the product chemistry data are attached (See Tables 1-2 and the CBI appendix).

1b. The manufacturing processes for metalaxyl and mefenoxam have been adequately described. The impurities are not likely to produce a residue problem.

2. The nature of the residue 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 methylester, expressed as metalaxyl equivalents.

3. The nature of the residue in animals is adequately understood. Residues of concern are metalaxyl, metalaxyl metabolites which may be converted to 2,6-dimethyl aniline (2,6-DMA), and metabolites containing the 2-hydroxymethyl-6-methyl aniline (HMMA) moiety.

4a. Residue field trials submitted as bridging data in support of the proposed registration of mefenoxam are adequate.

4b. Residues from the proposed use of mefenoxam, expressed as the combined residues of metalaxyl and its regulated metabolites (expressed as metalaxyl), are not expected to exceed existing tolerances for residues of metalaxyl.

4c. Processing data submitted for metalaxyl are adequate to support the proposed use of mefenoxam. There is no reasonable expectation that residues of mefenoxam in processed commodities will exceed the current tolerance levels for metalaxyl.

4d. Significant animal feed items are involved in the proposed uses of mefenoxam on several agricultural crops, but residues of mefenoxam in plant commodities are expected to be lower than current metalaxyl residues. Secondary residues in animal commodities resulting from the proposed use of mefenoxam are <u>not</u> expected to exceed current tolerances for metalaxyl in animals.

5a. Adequate enforcement methods are available for plant commodities in the FDA Multiresidue Protocol D (PAM, Vol. I Section 232.4).

5b. The current submission demonstrates that adequate recoveries for mefenoxam may be expected when Ciba-Geigy's method AG-395 is used.

5c. Analytical reference standards for mefenoxam and metalaxyl are available from the Pesticides and Industrial Chemicals Repository, RTP, NC.

6a. A revised Section B is needed with a rotational crop restriction for the proposed Mefenoxam LS and Mefenoxam E labels, similar to the restriction on the Mefenoxam G, -MC, and -WP labels.

6b. The label should be revised to restrict the use of mefenoxam and metalaxyl concurrently on the same crop.

7a. The storage stability data for mefenoxam provided in this submission adequately support the field trial data, however only frozen storage temperature for lettuce was provided. The temperature of frozen storage should be provided for the other samples, also.

7b. Storage stability data required in the Metalaxyl RED to support processing studies and analyses for livestock commodities, poultry tissues and eggs, are also required for mefenoxam.

8. Deficiencies listed in the Metalaxyl RED concerning analysis and recovery of HMMA-containing metabolites in poultry tissues and eggs should be addressed for mefenoxam.

9. The chemical name of the hydroxy metabolite should be corrected in 40 CFR 180.408 (a) and (c), 185.4000 (a), and 186.4000 (a), to, "N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl) alanine methyl ester." (See Metalaxyl RED by Sue Hummel, 6/19/94).

10. Harmonization between U.S., CODEX, and Canadian tolerances for metalaxyl is not currently possible because CODEX and Canadian tolerance expressions include only parent compound.

RECOMMENDATIONS

Pending receipt of a revised Section B (Conclusions 6a, 6b) and additional storage stability data (Conclusion 7a), CBTS can recommend for the registration of mefenoxam on crops registered currently for metalaxyl, provided mefenoxam is used at half the rate currently used for metalaxyl, and application is made in the same way as for metalaxyl. Existing tolerances for metalaxyl will be adequate to support the proposed uses of mefenoxam. The label should restrict the use of both pesticides concurrently on the same

crop. Deficiencies cited in Conclusions 7b, 8, and 9 may be resolved under reregistration.

A DRES run may be initiated using established metalaxyl tolerances. At such time when metalaxyl products are no longer available and only mefenoxam end use products are used, CBTS recommends that the Registrant petition for lower tolerances.

DETAILED CONSIDERATIONS

PRODUCT CHEMISTRY

The manufacturing process for technical grade mefenoxam has been adequately described, and all data requirements have been met. There are no impurities present in the technical grade mefenoxam products which are expected to cause residue concerns. All of the inerts have been cleared for use. A review of product chemistry is included in the attached Tables 1-2 and confidential appendix.

PROPOSED USE

Ciba-Geigy proposes use of mefenoxam on all plant commodities for which metalaxyl is registered [See 40 CFR 180.408 (a) and (c), 185.4000 (a), and 186.4000 (a)]. Numerous agricultural crops have registered uses. Proposed mefenoxam labels reflect maximum application rates which are exactly half those for metalaxyl. Identical application methods were used for metalaxyl and mefenoxam, i.e., ground or aerial, type of application equipment used, etc. The proposed uses for mefenoxam formulations for life-stage of application, lb. product used per acre, number of applications, application interval, preharvest interval and seasonal maximum, vary widely with the crop treated, as is the case for metalaxyl.

Mefenoxam labels were supplied for the following formulations (EPA file symbol numbers given in parentheses): Mefenoxam/copper (100-INU) and Mefenoxam/Bravo (100-INN), as well as the following mefenoxam formulations, *mefenoxam*: E (100-TOG), LS (100-TOO), MC (100-TOA), GR (100-TOI), 45WP (100-TOT), MZ (100-ING), EC (100-INR), PC liquid (100-801), PC (100-TOE), WP (100-TOL), WSP (100-INE), and G (100-TOU). Differences between proposed mefenoxam labels and current metalaxyl labels were listed. Significant changes to the label include replacing the old names with mefenoxam and decreasing the maximum proposed mefenoxam rate to half that currently registered for use for metalaxyl. Detailed mixing instructions were added, and other minor changes made, which would not have a significant impact on the current chemistry review.

Most of the proposed mefenoxam labels included the new 12 month restriction against planting any crop, **intended for food or feed**, which is not registered for use with mefenoxam-treated soils. They also stated that crops **not intended** for food or feed may have 0

days between planting time and last mefenoxam application. No rotational restriction was included on the Mefenoxam LS, -E, or -45W (a seed treatment use) label. The Mefenoxam G, -MC, and -WP labels stated only, "Do not plant any food crop which is not registered for use with mefenoxam in mefenoxam-treated soil for a period of 12 months." A similar rotational restriction statement is needed for the proposed Mefenoxam LS and E formulations.

Proposed labels for mefenoxam include a reduction of maximum mefenoxam rates of application to 1/2 those of metalaxyl, and frequently less than 1/2 the metalaxyl use rate when minimum mefenoxam rates are to be used, name changes from the metalaxyl product name, updated detailed mixing instructions, and other changes which are not directly pertinent to Chemistry. The name of the proposed mefenoxam formulation, the MRID numbers of submissions involving each mefenoxam formulation, and the corresponding metalaxyl formulation, are given in Table 1, entitled, "Proposed mefenoxam names, MRID's, and metalaxyl names."

TABLE 1: PROPOSED MEFENOXAM NAMES, MRID'S, AND METALAXYL NAMES

MEFENOXAM NAMES	MRID'S	METALAXYL NAMES
Mefenoxam E	438003-65, -70	Subdue 2E (100-619)
Mefenoxam LS	438003-77 to -82	Apron FS (100-684)
Mefenoxam MC	438003-71 to -76	Subdue 2E (100-619)
Mefenoxam GR	438003-53 to -58	Ridomil 5G (100-628)
Mefenoxam 45W	None listed	Apron 50W (100-738)
Mefenoxam MZ	438003-59, -64	Ridomil MZ72 (100-767)
Mefenoxam EC	438003-65, -70	Ridomil EC (100-607)
Mefenoxam PC Liquid	438003-65, -70	Ridomil PC Liquid (Ridomil 2E & PCNB 20E Liq. EC)
Mefenoxam PC	438003-35, -40	Ridomil PC 11G
Mefenoxam WP	438003-41 to -46	Subdue & WSP (100-718) & Subdue II (100-717)
Mefenoxam WSP	438003-41, -46	Ridomil 50W (100-735)
Mefenoxam/Bravo	438003-24, -29	Ridomil/Bravo 81W (100- 658)
Mefenoxam	438003-47, -52	Subdue Granular Fungicide (100-767).

NATURE OF THE METALAXYL/MEFENOXAM RESIDUE IN PLANTS (refer to 6/16/94 Metalaxyl RED Chapter by Sue Hummel)

The nature of the metalaxyl residue in plants is adequately understood. Studies on potatoes, lettuce, grapes, and tobacco indicate that metalaxyl is taken up, translocated, and extensively

metabolized by plants. Metabolism involves oxidation of the ring-methyl group and hydrolysis of the methyl ester and methyl ether bonds; metabolites can be conjugated to glucose. Studies with [^{14}C]metalaxyl-treated seed indicate that no appreciable residue was transferred from treated seed to edible mature plant parts. Residues regulated in plant commodities are defined by the current tolerance expression, including metalaxyl, metabolites that can be converted to 2,6-dimethyl aniline (2,6-DMA), and one metabolite containing the 2-hydroxymethyl-6-methyl aniline (HMMA) moiety, **N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl) alanine methyl ester.** The chemical name of the hydroxy metabolite (in **bold** type in the previous sentence) should be corrected in 40 CFR 180.408 (a) and (c), 185.4000 (a), and 186.4000 (a).

NATURE OF THE METALAXYL/MEFENOXAM RESIDUE IN ANIMALS

The nature of the residue in animals is adequately understood. The HED Metabolism Committee (9/10/93) has determined that the residues to be regulated in livestock commodities are metalaxyl, metabolites that can be converted to 2,6-dimethyl aniline (2,6-DMA), and those containing the 2-hydroxymethyl-6-methyl aniline (HMMA) moiety.

ANALYTICAL/ENFORCEMENT METHODS (See Metalaxyl RED)

Adequate enforcement methods are available to analyze plants for residues of metalaxyl and its regulated metabolites. Methods I and II in PAM, Vol. II correspond to Methods AG-348 and AG-349. Method AG-395, an improved version of AG-348, is an Agency-validated method for plant matrices.

Metabolites recently identified in livestock commodities are not included in the current metalaxyl tolerance expression. New validation data are required to show Method AG-576 adequately recovers metabolites containing the 2,6-DMA moiety and HMMA containing metabolites, as 2,6-dimethyl aniline. Method AG-576 is a combination of Agency validated Methods II in PAM, Vol. II and AG-395; both component methods of AG-576 adequately recover metalaxyl, per se.

However, additional data are required to demonstrate the recovery of HMMA-containing metabolites as 2,6-dimethyl aniline by the livestock tolerance enforcement method. The wording of the tolerance expression will depend on the recovery of HMMA-containing metabolites, using the current enforcement method. This issue will be resolved under the reregistration process.

Metalaxyl, per se, is completely recovered (>80%) using FDA Multiresidue Protocol D (PAM, Vol. I Section 232.4) [*Source: PESTDATA, PAM, Vol. I, Appendix, 8/93*].

ANALYTICAL METHOD

Residues of mefenoxam on lettuce, tomatoes, potatoes, tobacco and cabbage, reported with field trials discussed below, were determined by Method AG-395. Briefly, residues are extracted in methanol:water and refluxed with methanesulfonic acid and then made basic, converting the residues of concern to the common moiety DMA. After cleanup, the DMA residues are analyzed using GC with a NP detector in the nitrogen mode. The limit of detection stated in previous reviews was 0.05 ppm (PP#1F3993, CBTS#9011, 6/19/91). A limit of quantification of 0.05 ppm (micrograms/gram) (the lowest fortification successfully recovered) was reported.

The efficiency of the method recoveries was determined using fortified control samples and, for lettuce only, fortified radioactive samples. Results are summarized in TABLE 2. TABLE 2 lists the crop tested, the level/range/mean/ standard deviation (SD)/Coeficient of Variation (CV)/number of samples (no.) of fortification/limit of detection and limit of quantification. Recoveries are acceptable, and average from 88% to 107% for mefenoxam and from 71 to 80% for metalaxyl.

TABLE 2: SUMMARY OF SAMPLE RECOVERIES SUBMITTED WITH THIS PETITION

CROP, Level Fortified	Recoveries mefenoxam	metalaxyl	Limit of Quantif.
Lettuce, 0.05 ppm to 5.0 ppm (Radio-active Validation)	Range 73-116% Mean: 88% SD: 16% CV: 19% no.: 6	70-93% 80% 8.4% 10%	0.05 ppm
Tomatoes, 0.05 ppm to 30.0 ppm	Range 68-116% Mean: 98% SD: 13% CV: 13% no.: 16	57-107% 80% 13% 16%	0.05 ppm
Potatoes, 0.05 ppm to 10 ppm	Range 67-137% Mean: 107% SD: 26% CV: 24% no.: 8	62-108% 80% 16% 20%	0.05 ppm
Tobacco, 0.05 ppm to 60 ppm	Range 70-107% Mean: 88% SD: 10% CV: 11% no.: 10	57-88% 71% 9.5% 13% 11	0.05 ppm
Cabbage. 0.05 ppm to 20 ppm	Range 63-127% Mean: 94% SD: 15.9% CV: 16.9% no.: 30	57-94% 72% 9.4% 13%	0.05 ppm

Method Validation: LETTUCE

Method validation was conducted using temperature, humidity and nutrient controlled, greenhouse-grown, potted head lettuce (Lactuca sativa) transplants. The test was conducted in Greensboro, NC, between May, 1995, and January, 1996. Radioactive mefenoxam or metalaxyl was foliarly sprayed one day after transplanting, and then 7, 14, and 21 days post first application to 10 plants each using the 1X and 2X rates of mefenoxam and the 1X rate of metalaxyl. Four applications of radioactive mefenoxam were made at 0.1 - 0.2 lb ai/A, for a total seasonal rate of 0.4-0.8 lbs. ai/A (the 1X-2X rates, respectively). Four foliar applications of radioactive metalaxyl were applied identically, except at 0.2 lb ai/A, for a total seasonal rate of 0.8 lbs. ai/A (the 1X rate for

metalaxyl). Immature and mature lettuce was harvested one and seven days after the fourth application of pesticide.

Plant samples were homogenized, screened through a 2mm Wiley Mill- along with dry ice, labeled and frozen. To determine the TRR's, a Harvey Oxidizer was used to combust the samples. Generated ^{14}C was captured in a liquid scintillation liquid and disintegrations per minute (DPM) were determined using liquid scintillation counting. Summary data for the 2X mefenoxam treatment on lettuce was provided, and all the raw data in TABLE 3 represent three replicate samples of treated lettuce.

TABLE 3: MEFENOXAM & METALAXYL TOTAL RADIOACTIVE RESIDUES, ON LETTUCE REPLICATE SAMPLES

LETTUCE CROP	MEFENOXAM (ppm DMA) (1X Rate, 0.4 lb ai/A/Season)	MEFENOXAM (ppm DMA) (2X Rate, 0.8 lb ai/A/Season)	METALAXYL (ppm DMA) (1X Rate, 0.8 lb ai/A/Season)
IMMATURE	0.814 0.861 1.002		2.468 2.835 2.293
MATURE	0.498 0.523 0.454		1.360 1.395 1.297
SUMMARY DATA REPORTED IMMATURE	1.57	3.17	3.77
MATURE	0.87	2.03	1.89
REPLICATE STATISTICS	NO.SAMPLES MIN MAX		NO.SAMPLES MIN MAX
IMMATURE LETTUCE	3 0.81 1.00		3 2.29 2.84
MATURE LETTUCE	3 0.45 0.52		3 1.30 1.40
	MEAN SD %CV		MEAN SD %CV
IMMATURE LETTUCE	0.89 0.098 11		2.532 0.28 11
MATURE LETTUCE	0.49 0.035 7.1		1.351 0.050 3.7

NOTE: *TRR=TOTAL RADIOACTIVE RESIDUES corrected for % Recovery; NO.=Number of Samples; SD=Sample Standard Deviation; %CV=Coefficient of Variation=(SD/Mean x 100%);

Mean and maximum residues on lettuce from the 1X application of mefenoxam were all less than residues from the 1X application of metalaxyl.

Analytical Method: Field Samples

Analytical method AG-395, FDA Multiresidue Protocol D (PAM, Vol. I Section 232.4) was employed for the analysis of total residues of mefenoxam and metalaxyl. Slightly modified extraction steps for mefenoxam and metalaxyl were used. Modifications were made to improve solvent extractions, to speed up and make the analyses more

efficient, and to eliminate unnecessary procedures. The modifications were very specific, according to the plant crop to be tested. Residues were determined as 2,6-d methylalanine (DMA) separation was accomplished using capillary columns. A Hewlett-Packard 5890 or 5880 gas chromatograph with a NPD detector (Nitrogen specific) was used for analysis.

GLN 171-4 (E): STORAGE STABILITY:

The current petition included a summary of storage stability data for metalaxyl from three studies, but provided no data to review. MRID Nos. 40534802, 40106601, 42919401 and 43446901 were cited, instead. The first study reported frozen (-15 C) stability of metalaxyl parent in fortified potatoes and tobacco for 12 months. It also reported stability of total residues of metalaxyl in field-treated, frozen, samples of potatoes and tobacco for 18 months. The second study reported freezer stability (exact freezer temperature not reported) of metalaxyl and five metabolites for 12 months on fortified strawberries, apples, cabbage, lettuce, and potatoes. The third study reported results from frozen storage (-20 C) of weathered field samples of cranberries, peppers, potatoes, and spinach. It reported that total residues of metalaxyl were stable in peppers, potatoes, and spinach for 39 months and cranberries for 38 months.

Samples were stored frozen for the following numbers of months, radiolabeled method validation crop-lettuce (1-3), tomatoes (1-5), potatoes (1-2), tobacco (1-4), and cabbage (1-5). Adequate storage stability data were provided to support residue field studies, for the purposes of this bridging petition. However, only frozen storage temperature for lettuce (-20 C) was provided. The temperature of frozen storage should be provided for the other samples, also. In addition, Metalaxyl RED requirements for processing and storage stability studies (e.g. oilseed, grain, livestock, and fruit or fruiting vegetables) are also required for mefenoxam. This requirement can be addressed in reregistration.

CROP FIELD TRIALS (MRID Nos. 438969-01, -02, -03, -04, and -05)

Field data were submitted in January, 1996, for lettuce, tomatoes, potatoes, tobacco, and cabbage. Locations used for the field trials, and the rates of application varied widely, depending on the crop tested.

The following tables summarize reside data reported for mefenoxam and metalaxyl, expressed as ppm 2,6-dimethylaniline, DMA. Residues of mefenoxam and metalaxyl were similar for comparable application rates; however, the proposed rates of application for mefenoxam are half or less than application rates currently used for metalaxyl.

FIELD TRIALS: TOMATOES

Five field trials were conducted at the 1X application rate for mefenoxam and metalaxyl on tomatoes, from March to December, 1995. Three trials were conducted in two counties of California, and two trials were conducted in a single Florida location. Samples of mature tomatoes (10), immature tomatoes (25), and tomato leaves (16), were tested, using samples grown to maturity under typical agricultural practices.

One 1X application of metalaxyl employed Metalaxyl 50WP for surface spray at planting and then post-directed in 7" band, followed by another application using Metalaxyl MZ72WP post-foliar broadcast. The other 1X metalaxyl application employed Metalaxyl 5G as a surface spray at planting and then post-directed in 7" bands.

One 1X mefenoxam application used the 45WP formulation as a surface spray at planting and then post-directed in a 7" band, followed by a post-foliar broadcast application using the Mefenoxam MZ68WP. The other 1X mefenoxam application employed Mefenoxam 2G for banded surface spray at planting and then post-directed in 7" bands. The PHI's observed were, for mature tomatoes, 5 days; for immature tomatoes, 0 days, 8 days, and 14 days; and for tomato leaves, 1 and 8 days.

TABLE 4 summarizes data for all mefenoxam and metalaxyl residues in/on tomato samples, the number of samples, minimum and maximum residues reported, the mean, the standard deviation and coefficient of variation. All maximum and mean concentrations of mefenoxam, at the 1X application rate, were less than the concentration of metalaxyl at the 1X application rate.

TABLE 4: *MEFENOXAM & METALAXYL RESIDUES ON TOMATO SAMPLES*

TOMATO CROP	MEFENOXAM (ppm DMA) (1X Rate, 0.23 & 0.73 lb ai/A/Season, at planting & foliar spray)	METALAXYL (ppm DMA) (1X Rate, 0.46 & 1.46 lb ai/A/Season,at planting & foliar spray)
STATISTICS	NO.SAMPLES MIN MAX	NO.SAMPLES MIN MAX
MATURE TOMATOES	10 <0.05 0.07	10 <0.05 0.09
IMMATURE TOMATOES	25 <0.05 0.13	25 <0.05 0.19
TOMATO LEAVES	16 <0.05 6.2	16 <0.05 12.
	MEAN SD %CV	MEAN SD %CV
MATURE TOMATOES	0.053 0.0068 13	0.060 0.014 23.
IMMATURE TOMATOES	0.057 0.02 35	0.068 0.04 59.
TOMATO LEAVES	2.0 2.0 100	4.1 4.1 100
INDIVIDUAL DATA REPORTED:		
MATURE TOMATOES	<0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 0.06 0.07	<0.05 <0.05 <0.05 <0.05 <0.05 <0.05 0.07 0.07 0.07 0.09
IMMATURE TOMATOES	<0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 0.06 0.07 0.12 0.13 <0.05 0.07 0.08 0.09	<0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 0.06 0.07 0.07 0.08 0.10 0.13 0.16 0.19
TOMATO LEAVES	0.65 0.74 1.3 1.6 1.6 1.8 2.0 2.1 4.0 4.7 5.0 6.2	<0.05 0.10 0.10 0.13 1.5 1.7 3.1 3.1 3.1 3.4 3.7 4.3 7.8 10 12 12

NOTE: Residues are corrected for % Recovery; NO.=Number of Samples; SD=Sample Standard Deviation; %CV=Coefficient of Variation= (SD/Mean x 100%)

FIELD TRIALS: POTATOES

Field trials were conducted in New York, Idaho, Washington, and North Dakota, using mefenoxam and metalaxyl on potatoes from April to December, 1995. Treatments used Ridomil 2E, CGA-329351 (mefenoxam) 4E, Ridomil MZ72, and CGA-329351 MZ68.

Four different treatment regimes were used. Treatment 1 was a control. Treatment 2 was a metalaxyl treatment using Ridomil 2E applied to soil at planting, at a rate equivalent to 2.0 lbs ai/A, plus four foliar applications of Ridomil MZ72 at 0.2 lb ai/A/application, at 14 day intervals.

Treatment 3 used Mefenoxam 4E for ground application and mefenoxam MZ68 foliarly at half the use rate observed for metalaxyl, in Treatment 2. Treatment 4 used four applications of Mefenoxam MZ68, foliarly applied, at 0.2 lb ai/A/application. Treatment 5 used four applications of Mefenoxam MZ68, foliarly applied, at 0.1 lb ai/A/application-equivalent to 1/2 the metalaxyl rate in Treatment 4.

Samples were grown to maturity under typical agricultural practices.

TABLE 5 summarizes data for mefenoxam and metalaxyl residues in/on potatoes (tubers) and potato leaf samples. No detectable residues of mefenoxam or metalaxyl were found on potato tubers, all reported residues were <0.05 ppm DMA. For potato leaves, the mean and maximum residues of mefenoxam (conducted at the 1X application rate) were all less than the residues of metalaxyl (conducted at the 1X application rate).

TABLE 5: MEFENOXAM & METALAXYL RESIDUES ON POTATO SAMPLES

POTATO CROP	MEFENOXAM (ppm DMA) (1X Rate, 4 X 0.1 lb ai/A/Season, foliar spray)	METALAXYL (ppm DMA) (1X Rate, 4 X 0.2 lb ai/A/Season foliarly, & 1.4-2.8 at planting & foliar spray)
STATISTICS	NO.SAMPLES MIN MAX	NO.SAMPLES MIN MAX
MATURE POTATO TUBERS	16 <0.05 <0.05	16 <0.05 <0.05
POTATO LEAVES	12 0.54 5.1	12 1.9 8.9
	MEAN SD %CV	MEAN SD %CV
MATURE POTATO TUBERS	<0.05 0	<0.05 0
POTATO LEAVES	2.6 1.6 62%	5.6 2.9 52%
INDIVIDUAL DATA REPORTED:		
MATURE POTATO TUBERS	<0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05	<0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05
POTATO LEAVES	0.54 0.78 0.92 1.2 1.9 2.4 3.0 3.1 3.7 4.5 4.7 5.1	1.9 2.0 2.7 2.8 5.8 6.6 7.3 7.4 8.0 8.5 8.5 8.9

NOTE: Residues corrected for % Recovery; NO.=Number of Samples; SD=Sample Standard Deviation; %CV=Coefficient of Variation=(SD/Mean x 100%)

FIELD TRIALS: TOBACCO

Field trials were conducted in Tennessee, North Carolina, Kentucky, and Virginia, using mefenoxam and metalaxyl on tobacco from March to November, 1995. For metalaxyl, three applications of Ridomil 50WP at 1.0 lb ai/A each were applied for a total of 3.0 lb ai/A/season. For mefenoxam, CGA-329351 (mefenoxam) 45P was applied at one half the use rate of metalaxyl, for a total of 1.5 lb ai/A/season. Metalaxyl (50WP) or Mefenoxam (45P) was applied preplant incorporated to the soil at the first application. The second application was post directed after the first cultivation. Finally, the third application was made, most directed, at lay-by. Tobacco was grown to maturity under normal agricultural practices. PHI's of 0, 33, 57, and 61 days were observed.

TABLE 6 summarizes the mefenoxam and metalaxyl residues in/on tobacco samples, number of samples, minimum and maximum residues reported, mean, standard deviation and coefficient of variation. Mean and maximum residues of mefenoxam on tobacco (1X application, 1.5 lb ai/A/season), were all less than the residues of metalaxyl (1X application, 3.0 lb ai/A/season).

TABLE 6: MEFENOXAM & METALAXYL RESIDUES ON TOBACCO SAMPLES

TOBACCO CROP	MEFENOXAM (ppm DMA) (1X Rate, 3 X 0.5 lb ai/A/Season = 1.5 lb ai/A/Season Added	METALAXYL (ppm DMA) (1X Rate, 3 X 1.0 lb ai/A/Season = 3.0 lb ai/A/Season Added
STATISTICS	NO.SAMPLES MIN MAX	NO.SAMPLES MIN MAX
TOBACCO LEAVES	16 0.23 13.	16 0.94 35.
	MEAN SD %CV	MEAN SD %CV
TOBACCO LEAVES	2.2 3.5 159%	5.3 9.3 175%
INDIVIDUAL DATA REPORTED:		
TOBACCO LEAVES	0.45 0.65 0.79 0.85 4.0 5.0 6.7 13	0.94 1.1 2.3 2.4 11. 11. 16. 35.

NOTE: Residues corrected for % Recovery; NO.=Number of Samples; SD=Sample Standard Deviation; %CV=Coefficient of Variation=(SD/Mean x 100%)

FIELD TRIALS: CABBAGE

Field trials were conducted in California, New York, Florida, and Texas, using mefenoxam and metalaxyl on cabbage from March to October, 1995. Cabbage was grown to maturity under normal agricultural practices. Treatments with metalaxyl 50WP to transplanted cabbages consisted of one application of 2.0 lbs ai/A preplant incorporated to the soil, plus four applications of 0.2

lbs ai/A, using post-foliar spray at approximately 14 day intervals, for a total treatment of 2.8 lbs ai/A/season. Treatments with Mefenoxam 45WP one application of 1.0 lbs ai/A preplant incorporated to the soil, plus four applications of 0.1 lbs ai/A, using post-foliar spray at approximately 14 day intervals, for a total treatment of 1.4 lbs ai/A/season. PHI's of 0 and 7 days were observed.

TABLE 7 summarizes mefenoxam and metalaxyl residues in/on cabbage samples, the number of samples, minimum and maximum residues reported, the mean, the standard deviation and coefficient of variation. For all cabbage samples, mean and maximum residues of mefenoxam (conducted at the 1X application) were all less than the residues of metalaxyl (conducted at the 1X application).

TABLE 7: MEFENOXAM & METALAXYL RESIDUES ON CABBAGE SAMPLES

CABBAGE CROP	MEFENOXAM (ppm DMA) (1X Rate, 1.0 & (4 X 0.1) lb ai/A/Season, at planting & foliar spray, total 1.4 lb ai/A/season)	METALAXYL (ppm DMA) (1X Rate, 2.0 & (4 x 0.2) lb ai/A/Season, at planting & foliar spray, total 2.8 lb ai/A/season)
STATISTICS	NO.SAMPLES MIN MAX	NO.SAMPLES MIN MAX
MATURE CABBAGE	16 <0.05 2.4	16 <0.05 7.3
CABBAGE WRAPPER LEAVES	20 0.11 3.5	20 0.10 15.
CABBAGE: TRIMMED HEADS	16 <0.05 0.41	16 <0.05 0.80
	MEAN SD %CV	MEAN SD %CV
MATURE CABBAGE	0.73 0.75 103%	1.8 2.1 117%
CABBAGE WRAPPER LEAVES	1.5 1.0 67%	3.5 4.4 126%
CABBAGE: TRIMMED HEADS	0.13 0.10 77%	0.25 0.20 80%
	INDIVIDUAL DATA REPORTED:	
MATURE CABBAGE		
0 DAY PHI	0.09 0.13 0.34 0.34 0.42 0.75 1.6 1.9	<0.05 <0.05 0.69 0.72 0.98 2.0 4.6 4.6
7 DAY PHI	<0.05 <0.05 0.23 0.33 0.58 0.84 1.7 2.4	<0.05 <0.05 0.40 0.59 1.5 2.0 2.7 7.3
CABBAGE WRAPPER LEAVES	0.46 0.66 1.4 1.4	0.21 0.27 0.30 0.43
0 DAY PHI	1.7 1.9 2.3 2.4 2.6 3.5	3.7 4.3 4.6 4.7 14. 15.
7 DAY PHI	0.11 0.14 0.37 0.53 0.87 1.0 2.2 2.2 2.3 2.6	0.10 0.14 0.16 0.16 1.2 1.4 3.2 3.3 4.9 7.7
CABBAGE: TRIMMED HEADS	0.09 0.11 0.19 0.20 0.23 0.41	0.12 0.14 0.34 0.42 0.44 0.80
0 DAY PHI	<0.05 <0.05 <0.05 <0.05 0.07 0.08 0.08 0.11	<0.05 <0.05 <0.05 <0.05 0.17 0.18 0.21 0.27
7 DAY PHI	0.16 0.18	0.31 0.38

NOTE: Residues corrected for % Recovery; NO.=Number of Samples; SD=Sample Standard Deviation; %CV=Coefficient of Variation=(SD/Mean x 100%

PROCESSING DATA

Processing study data were not submitted for mefenoxam, however, there is no reasonable expectation that mefenoxam should concentrate differently than metalaxyl during processing. There is no reasonable concern that residues of mefenoxam in processed commodities will exceed the current tolerance levels for metalaxyl.

SECONDARY RESIDUES IN MEAT AND MILK

There are significant animal feed items which would be involved following the proposed use of mefenoxam on several crops. However, there is no reasonable expectation that secondary residues of mefenoxam in livestock or poultry, meat byproducts, fat, milkfat, whole milk, or eggs will exceed the current tolerance levels for metalaxyl.

CODEX

Harmonization between U.S., CODEX and Canadian tolerances for metalaxyl is not possible at this time since the CODEX and Canadian tolerance expressions include only the parent compound.

cc: RF, Mefenoxam SF, Metalaxyl SF, Metalaxyl Reg Std File,
L. Kutney, E. Haeberer, Connie Welch, RD; Kathryn Scanlon, RD;
cc without Confidential Appendix: Circu, Beth Doyle (DRES-SAB)
CM2:305-5351:RM816G:7509C:LLKutney:llk-**4/23/96**,
RDI: E. Haeberer:4/21/96, Loranger:4/22/96

REVIEW OF PRODUCT CHEMISTRY (SUBDIVISION D), GLN'S 61 TO 63

Product Chemistry Table 1: Manufacturing and Impurity Data for MEFENOXAM, REG. NUMBER: 100-791, (TEST SUBSTANCE/PRODUCT: PAI/TGAI [1].

GLN	MRID	Status[2]	Deficiency[3]
61-1: Product Identity & Disclosure of Ingredients	42409201 234427 41912901	A	No % of S enantiomer listed on Statement of Formula (92% minimum listed for both R and S enant.) On CSF (S-enant. is 0-4%) & R-enant. is 91%-98%. Minimum % on CSF is lower! Both CAS' on CSF or CGA's for impurities
61-2: Starting Materials & Manufacturing Process	41055201 41912901	A	
61-3: Discussion of Impurities	41055201 41912901	A	
62-1: Preliminary Analysis	41055202 42319901	A	
62-2: Certification of Limits	41055202 41912901 42409202	A	
62-3: Analytical Methods	41055202 42319901	A	

[1] For example, test substance might be PAI and product might by 95% technical MP.
[2] A = Acceptable, N = Unacceptable (see Deficiency).
[3] Refer to CBI Appendix A for details.

Product Chemistry Table 2: Physical and Chemical Properties for (NAME), (REGISTRATION NUMBER)			
GLN	MRID	Status[1]	Result[2] or Deficiency
63-2: Color	234427	A	Pale Yellow PAI/TGAI
63-3: Physical State	234427	A	Clear, Viscous Liquid PAI/TGAI
63-4: Odor	234427	A	Weak Odor PAI/TGAI
63-6: Boiling Point	234427	A	>270 C for PAI
63-7: Density, Bulk Density, or Specific Gravity	234427	A	1.125 g/cm^3 for TGAI typical at 20 C
63-8: Solubility	234427	A	Water 26 g PAI/l n-hexane 59 g TGAI/l TGAI is Completely miscible in: Methanol, Acetone, Toluene, n-Octanol, Ethylacetate, dichloromethane
63-9: Vapor Pressure	234427	A	3.3 x 10^{-3} Pa @ 25 C for PAI
63-10: Dissociation Constant	234427	A	PAI had no dissociation constant in pH 1-10 range, using UV-spectrum Method at different pH's.
63-11: Octanol/Water Partition Coefficient	Jacoby letter 3/17/82	A	log Pow = 1.71 @ 25 C
63-12: pH	Jacoby letter 3/17/82	A	TGAI has pH of 5-6 @ 25 C (1% aqueous dispersion-ASTM E 70-77)
63-13: Stability	234427	A	% Decomposition in Sunlight (tested with xenon arc lamp) = 3% in one Day. @ Room Temp and 38 C, TGAI showed <1% decomposition, when contacting zinc, aluminum or copper. TGAI in contact with iron, showed 1% decomp. at RT and 3% at 38 C. TGAI Stable to carbon and stainless steel, aluminum and tin at 37 C and RT for 1 month, showing only up to 1% decomposition.
63-14: Oxidizing or Reducing Action	Jacoby letter 3/17/82	A	No oxidizing or reducing properties reported, using Method EEC A.17.
63-15: Flammability	Jacoby letter 3/17/82	A	Flash Point 179 C (method A.10) Auto Ignition Temp 410 C (method A.15)
63-16: Explodability	Jacoby letter 3/17/82	A	Not explosive, based on test results (method EEC A.14) for thermal sensitivity and mechanical sensitivity.
63-17: Storage Stability	Jacoby letter 3/17/82	?	In Progress-Work with commercial packaging

63-18: Viscosity		A	TGAI tested using OECD #115. At 20 C: 2800 $\pm$ 100 mPa • S at shear rate D = $0.1710 < D < 0.794\ S^{-1}$ At 40 C: 311.5 $\pm$ 6.3 mPa • S at shear rate D = $1.995 < 6.81\ S^{-1}$
63-19: Miscibility		A	Report in 63-8
63-20: Corrosion Characteristics	234427	A	TGAI & test container unchanged after 1 month storage.
[1] A = Acceptable; N = Unacceptable (see Deficiency); N/A = Not applicable. [2] For example, "brown" for 63-1; "155° C" for 63-4.			

(Ciba Lists 63-21 Dielectric Breakdown Voltage as N/A)

Page _____ is not included in this copy.

Pages __21__ through __23__ are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

__X__ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

_____ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

__ _ __ Internal deliberative information.

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_____ Claimed Confidential by submitter upon submission to the Agency.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
