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

SEP 26 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F3387/6H5499 Metalaxyl on Fruiting Vegetables (except Cucurbits), Sugar Beets, and Sugar Beet Tops Evaluation of Analytical Method and Residue Data (Accession Numbers 262111 and 262112) [RCB Numbers 768 and 769]

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and

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THRU: Charles L. Trichilo, Chief
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Ciba-Geigy Corporation proposes tolerances for residues of the fungicide metalaxyl, trade named Ridomil® and Apron® [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 or on the following raw agricultural commodities (RAC's):

Fruiting Vegetables (except Cucurbits) at 1.0 ppm,
Sugar Beets and Sugar Beet Tops at 0.1 ppm.

In addition, Ciba-Geigy is also requesting the establishment of a feed additive tolerance for combined residues of metalaxyl and its above named metabolites in or on the following processed commodity:

Dry Tomato Pomace at 20.0 ppm.

Metalaxyl and its metabolite tolerances are established on a variety of RAC's ranging from 0.02 ppm in milk, 0.05 ppm in meat and eggs, 0.1 ppm in poultry to 1.0 ppm in tomatoes, squash, cucumbers, and 10 ppm in green onions (see 40 CFR 180.408). Combined metalaxyl tolerances are also established for animal feed items ranging from 4.0 ppm in dried processed potato waste to 16 ppm in dry tomato pomace (see 21 CFR 561.273). Temporary tolerances for combined residues of metalaxyl in wet tomato pomace at 5 ppm and dry tomato pomace at 20 ppm expired on January 1, 1984. Food additive tolerances are also established for combined residues of metalaxyl and its metabolites in processed tomatoes at 3.0 ppm to 4.0 ppm in processed potatoes (including potato chips) (see 21 CFR 193.277).

The fruiting vegetables (except cucurbits) group is defined in 40 CFR 180.34(f)(9)(viii). Representative commodities for this grouping as stated in the above reference are tomatoes and peppers (including bell peppers, chili peppers, cooking peppers, pimentos, and sweet peppers). Some other members of fruiting vegetables (except cucurbits) group are eggplants, ground cherries, and tomatillos.

Metalaxyl was the subject of a Registration Standard issued in December 1981. There are no outstanding deficiencies that need to be addressed in this petition.

A proposed temporary metalaxyl tolerance in or on grapes and grape byproducts has received a favorable RCB recommendation (see memorandum PP#4G3031/FAP5425, L. Cheng, June 3, 1986) while a proposed permanent tolerance for metalaxyl in or on grapes is currently in reject status (see memorandum 6F#3362/FAP#6H5493, M.P. Firestone, March 20, 1986). A proposed metalaxyl tolerance on strawberries at 5 ppm is also currently in reject status (see memorandum PP#6F3337, M.P. Firestone, February 21. 1986).

RCB has recommended favorably for metalaxyl on asparagus at 7 ppm (see memorandum PP#6F3330 M.P. Firestone, February 7, 1986) and on raspberries at 0.5 ppm (see memorandum PP#3F2848, M.J. Nelson, July 6, 1983).

RCB has previously recommended for, and a tolerance has been established for metalaxyl on fruiting vegetables (except cucurbits) group (except tomatoes) at 0.1 ppm (see memorandum PP#3F2827, P.V. Errico, November 2, 1983). This tolerance proposal was based on a seed treatment use.

Conclusions

1a. The petitioner needs to submit a revised Section B (new Ridomil® label) which has a seven-day pre-harvest interval (PHI) for the fruiting vegetables (except cucurbits) group.

1b. RCB suggests the petitioner add a label caution stating that prior to mixing with any proposed tank mates, check each label to be sure the proposed uses are compatible for the fruiting vegetables (except cucurbits) group, and that there are labeled uses for the proposed tank mate(s) on the fruiting vegetables (except cucurbits) group.

2. The nature of the residue in plants and animals is adequately understood for purposes of supporting the proposed metalaxyl use on the fruiting vegetables (except cucurbits) group and sugar beet roots and tops. The residues of concern are metalaxyl, its metabolites containing the 2,6-dimethylaniline (DMA) moiety and N-[2-(hydroxymethyl)-6-methylphenyl]-N-(methoxyacetyl) alanine, methyl ester.

3a. Enforcement methods for metalaxyl are in the Pesticide Analytical Manual (PAM-II) as of November 1984.

3b. RCB cannot judge the adequacy of these methods to gather metalaxyl residue data on the fruiting vegetables (except cucurbits) group without supporting chromatographic data (see Analytical Methods discussion following).

4a. RCB concludes the petitioner has presented sufficient geographically representative residue data and that metalaxyl and its 2,6-DMA metabolite residues on tomatoes from the proposed uses will not exceed the requested crop group tolerance of 1 ppm.

4b. To help prevent a proliferation of tolerances, RCB suggests the petitioner submit one feed additive metalaxyl tolerance for tomato pomace in a revised Section F as follows:

Tomato Pomace (wet or dry) 20 ppm.

4c. RCB concludes and that the petitioner has presented adequate variety and sufficient geographically representative data, and that metalaxyl and its 2,6-DMA metabolite residues on peppers from the proposed uses will not exceed the requested crop group tolerance of 1 ppm.

4d. Adequate representative crop residue data for the crop grouping fruiting vegetables (except cucurbits) are submitted. Residues for this crop grouping are not expected to exceed the proposed 1 ppm tolerance.

4e. Metalaxyl and its 2,6-DMA metabolite residues in sugar beets and sugar beet tops will not exceed the proposed 0.1 ppm tolerance from the proposed seed treatment use.

4f. The petitioner needs to conduct a processing study for sugar beets containing metalaxyl residue and present the results for the processed commodities and feed items showing the metalaxyl concentration factors. Also, the petitioner may need to propose additional food and feed additive tolerances depending on the outcome of the proposing processing study.

5. When the various feed items are included in an artificial diet, the established secondary metalaxyl tolerances in milk, eggs, meat, fat, and meat byproducts of cattle, goats, hogs, horses, sheep, and poultry are adequate and will not be exceeded from the proposed uses in this petition.

6. An International Residue Limit status sheet is attached to this petition. There is a Codex tolerance for the parent fungicide only on tomatoes. Since the U.S. has objected to the exclusion of metalaxyl metabolites in the tolerance expression, Codex may in a future meeting reconsider its metalaxyl metabolites exclusion from the tolerance expression.

<u>Note to PM</u>: If and when the tolerances requested in this petition are established, the existing metalaxyl tolerances on tomatoes at 1 ppm and on fruiting vegetables (except cucurbits) group (except tomatoes) at 0.1 ppm in 40 CFR 180.408 should be deleted. These tolerances will be replaced by the newly established crop group tolerance of 1.0 ppm metalaxyl for 40 CFR 180.408.

Recommendation

RCB cannot recommend, at this time, for the requested metalaxyl tolerances on the fruiting vegetables (except cucurbits) group at 1 ppm, and sugar beets and sugar beet tops at 0.1 ppm from the proposed uses for the reasons cited in conclusions la, lb, 3b, 4b, and 4f.

For further consideration the petitioner should be advised to do the following:

1. Present a revised Ridomil® label in a new Section B as suggested in conclusions la and lb.

2. Provide photocopies of the requested supporting chromatographic data as suggested in conclusion 3b.

3. Present a revised Section F for a metalaxyl tolerance on tomato pomace as suggesed in conclusion 4b.

4. Conduct a metalaxyl on sugar beets processing study and propose the necessary, if any, feed and food additive tolerances in a revised Section F as suggested in Conclusion 4f.

Detailed Considerations

Manufacture and Formulation

The manufacturing process for metalaxyl has been adequately described and previously discussed (see memorandum PP#1F2500, P.V. Errico, March 9, 1982). Impurities in the technical mixture are not expected to present a residue problem (see memorandum PP#8G2121, G. Makhijani, March 29, 1979).

The formulation proposed for use on the fruiting vegetables (except cucurbits) group in Ridomil® 2E, an emulsifiable concentrate that contains two lbs active ingredient (ai) or 25.1% ai/gallon (EPA Registration No. 100-607). The inert ingredients for Ridomil® 2E are exempt from the requirement of a tolerance under 40 CFR 180.1001(c) and (d). The Confidential Statement of Formula (CSF) dated September 18, 1979 is filed with PP#1F2500 and a revised CSF, dated March 17, 1982, is in RD.

The formulation proposed for use on sugar beet seed is Apron® 25W, a wettable powder containing 25% active ingredient (EPA Registration No. 100-639). The inert ingredients are exempt from the requirement of a tolerance under 40 CFR 180.1001(c) and (d). The CSF dated August 30, 1982, is filed with RD.

Proposed Uses

Ridomil® is proposed as a systemic fungicide to control diseases in crops caused by the Oomyate class of fungi, i.e., pyrthium damping off and phytophthora crown rot.

Ridomil® is proposed for a band spray soil application over pepper and eggplant rows at seeding time with a 1.0 lb ai/acre application rate. Two additional post-directed applications of Ridomil® at 0.5 lb ai/acre are proposed. A 30-day spray interval between applications is proposed. No PHI is recommended. On page one of the summary in Section D the petitioner states a seven-day PHI is proposed yet we are unable to locate this on the proposed label. RCB suggests a seven-day PHI is appropriate based on our review of the residue data. The petitioner warns the user of potential phytotoxicity problems. Ridomil® should not be applied foliarly for control of phytophthora blight.

For tomatoes apply Ridomil® at a rate of four to eight pints (one to two lbs ai)/acre in 20 to 50 gallons of water as a broadcast soil surface spray at planting. Incorporate the Ridomil® either mechanically or by irrigation. Ridomil® could also be applied four to twelve weeks prior to harvest as a surface application at the rate of 1.0 lb ai (four pints)/acre. Since tomatoes can be harvested over an extended period RCB suggests the same seven-day PHI as proposed for pepper and eggplants is appropriate for tomatoes.

For the fruiting vegetables (except cucurbits) group do not apply more than 3.0 lb ai (twelve pints) of Ridomil®/acre/season.

In the General Information section of the label under mixing instructions the petitioner states Ridomil® is usually compatible with a number of other pesticides. RCB suggests the petitioner add a caution statement that prior to mixing with any proposed tank mate check each label to be sure the proposed uses are compatible and there is a label recommended use for that pesticide on the members of the fruiting vegetables (except cucurbits) group.

Apron® 25 is proposed as a fungicide seed treatment chemical to control systemic downy mildew, seed rot, and damping-off. Apron® is to be used only by commercial seed treaters. Apron® is to be applied to sugar beet seed as a water based slurry at a rate of two ounces (0.5 oz ai)/100 lbs of seed. The label has the following restriction: Use with an EPA approved dye that imparts an unnatural color to the seed. Seed treaters are warned that any bags of treated seed must contain the following statement "This seed has been treated with metalaxyl fungicide. Do not use for feed, food, or oil purposes. Store away from feeds and foodstuffs."

Nature of the Residue

Plant Metabolism

No new plant metabolism studies were submitted. Radiolabeled metabolism studies using phenyl ring ^{14}C-metalaxyl on potato, grape, and lettuce have been previously submitted and adequately reviewed (see memoranda PP#1F2500, P. Errico, March 9, 1982, and PP#8G2121, G. Makhijani, March 29, 1979). Additional plant metabolism studies of metalaxyl on lettuce and spinach have also been previously submitted and adequately reviewed (see memorandum PP#2F2762, N. Dodd, December 8, 1983).

In summary, metalaxyl in plants is metabolized through one or more of the following processes: oxidation of the ring methyl to benzyl alcohol/benzoic acid, hydroxylation of the phenyl ring, hydrolysis of the methyl ester, cleavage of the methyl ether, N-dealkylation and subsequent conjugation of some of the metabolites.

The fate of metalaxyl in plants is adequately understood. The residues of concern are metalaxyl, its metabolites containing the 2,6-dimethylaniline (DMA) moiety and N-[2-(hydroxymethyl-6-methylphenyl]-N-(methoxyacetyl) alanine, methyl ester.

Animal Metabolism

Radiolabel metabolism studies in rats, goats, and cows have been previously studied and adequately reviewed (see memoranda PP#86212, G. Makhijani, March 29, 1979, and PP#1F2500, P. Errico, July 15, 1982).

In summary metalaxyl is rapidly excreted in the urine and feces. From the studies we conclude metalaxyl degradation in animals follows the same mechanism as in plants, i.e., methyl ester hydrolysis, N-dealkylation, methyl ether cleavage, benzylic methyl oxidation with subsequent formation of glucuronic acid conjugates. In the lactating goat, small amounts of radioactivity were detected in the milk, blood, and tissues.

The fate of metalaxyl in meat and milk is adequately understood. The residues of concern are metalaxyl, and metabolites containing the 2,6-dimethylaniline (DMA) moiety, and N-[(2-hydroxymethyl)-6-methylphenyl]-N-(methoxyacetyl)alanine, methyl ester.

No poultry metabolism studies are available. RCB has previously considered the nature of the residue in poultry to be adequately understood by translation of the above animal studies. Poultry studies are normally required. Present studies show metalaxyl residues to be low in most tissue and transitory in liver and kidney. Since there are no major poultry feed items associated with this petition RCB will not pursue the issue further at this time.

Analytical Methods

The petitioner used four analytical methods to generate the metalaxyl and its metabolite data submitted with this petition.

The method used to gather most of the metalaxyl residue data on tomatoes is titled "The Determination of CGA-48988 and Its Metabolites in Tobacco as 2,4-Dimethylaniline Using Phosphoric Acid Reflux." The method is dated November 7, 1978, by K. Balasubramanian and W.B. Nixon. The method number is AG-330. The method has been previously submitted and reviewed (see memorandum PP#1F2500, P.V. Errico, March 9, 1982). A modified version of the method dated November 25, 1980, by K. Balasubramanian, entitled "Analytical Method for the Determination of Total Residues of Metalaxyl in Crops as 2,6-Dimethylaniline" has had a successful method tryout (see memorandum PP#1F2500, November 26, 1982, C. Corley) and is Method I in PAM-II as of November 1984. This version is coded AG-348. EPA recoveries using this method to determine total metalaxyl in cottonseed ranged from 45 percent to 72 percent at a 0.1 ppm spike level.

The method used to gather the metalaxyl residue data on peppers is coded AG-395, dated December 7, 1982, by K. Balasubramanian and R. Perez and titled "Improved Method for the Determination of Total Residues of Metalaxyl in Crop as 2,6-dimethylaniline." This method has been previously submitted and reviewed (see memorandum PP#3F2918, K. Arne, December 13, 1983). RCB judged the method to be significantly different from methods 330 and 348, thus a method tryout (MTO) was requested. The results of the MTO (see memorandum PP#3F2918, P. Jung, July 9, 1984) showed EPA recoveries of total metalaxyl from peanuts and peanut hay range from 62 percent to 102 percent at spike levels of 0.05 ppm, 0.5 ppm, and 5 ppm. The method has been submitted to FDA but is not presently in PAM-II.

A suitable enforcement procedure exists for total metalaxyl residues in liver and milk. The method also has had a successful MTO (op. cit.) and is in PAM-II as of November 1984, as

Method II. The milk and liver (tissue) method is a modification of the tobacco method. The method is coded AG-349. This method is essentially the same as method 348 except with different extraction solvents before hydrolysis: acetonitrile (ACN) for milk, 80% aqu.. ACN for tissues, and hexane for eggs. The limit of metalaxyl detection is milk is 0.01 ppm, in liver and kidney at 0.1 ppm, and 0.05 ppm in eggs. Milk spiked at 0.01 ppm to 0.1 ppm total metalaxyl had recoveries ranging from 52 percent to 76 percent and bovine liver samples spiked with metalaxyl at 0.1 ppm to 0.4 ppm had recoveries ranging from 54 percent to 116 percent. Similar recoveries were noted for eggs and poultry products.

The petitioner has submitted ^{14}C-metalaxyl validation data for methods AG-330, AG-348, and AG-395. Method AG-330 was validated by using ^{14}C-metalaxyl field incurred residues in tobacco. Analysis by AG-330 accounted for 52 percent to 68 percent of the extractable residue. The ^{14}C-metalaxyl method validation data for AG-348 and AG-395 has been previously submitted and adequately reviewed (ibid.). In summary, method AG-395 was validated by analyzing mature lettuce harvested zero and seven days after application of ^{14}C-metalaxyl at the maximum label rate. The method accounted for 78 percent of the activity at day zero and 62 percent of the activity at seven days PHI. Method AG-348 was also validated by analyzing mature lettuce leaves after treatment with ^{14}C-metalaxyl. 73 percent of the activity was accounted for on day zero but a lower percentage activity was accounted for at day seven (48%).

The petitioner presented the results of two interference studies; one for method AG-330 and the other for method AG-348. The studies were conducted by adding to potatoes, tolerance level amounts of 64 pesticides registered for use on potatoes then analyzing the samples for metalaxyl equivalents. Method AG-330 showed no metalaxyl equivalents except for CIPC. The petitioner claimed this interference could be eliminated in the GC/MS confirmation step by having the GC/MS operated in the CI mode using SIM for the fragment ion at m/e 230. In method AG-348 none of the pesticides tested showed metalaxyl equivalents on the chromatograms to the 0.05 ppm screening level.

While it appears the petitioner has adequately validated his method used to gather the residue data in this petition, RCB defers judgment until it has reviewed the supporting chromatographic data (see below).

Briefly, method AG-330 involves blending 15 grams of tomatoes in 300 mL of methanol/water (4/1) for ten minutes. An aliquot (one or five gms) is evaporated on a roto-evaporator to < 5 mL but not dryness. The sample is refluxed 16 hours in 85 percent H_3PO_4 and one gram of $CaCl_3 \cdot 6H_2O$. After cooling, the solution is made basic with 200 mL of 25 percent NaOH to a pH > 5. The 2,6-dimethylaniline is steam distilled into 15 mL of hexane. The steam distillation apparatus is a modification of the equipment proposed by Veith and Kiwus. The distillation time is approximately 1 1/4 hours. The hexane is drawn off, dried over anh. Na_2SO_4. 100 uL of trichloroacetylchloride is added to form the derivative. The derivative is washed 2 x 25 mL 5 percent $NaHCO_3$ then cleaned up on an alumina column, Woelm, basic, grade V. The derivative is eluted off the column in the 150 mL hexane fraction then the hexane is rotoevaporated to dryness in a water bath no higher than 30 °C. The sample is made to 5.0 mL volume in acetone then analyzed by GC. The instrument used was a Tracor Gas Chromatograph, model 200, equipped with an alkali flame detector and a 1.2 m x 4 mm(id) glass column packed with 3 percent Dexsil-300 on Gas Chrom Q operated at 155 °C and a He carrier gas at 60 mL/min. The limit of detection is 0.05 ppm to 0.1 ppm. Quantitation is either peak height or peak area comparison of the unknown to knowns on a standard curve. Samples were corrected for recovery and a factor of 1.053 is used to connect residues of TCA-DMA detected to metalaxyl equivalents. With n = 31 metalaxyl recoveries in tomatoes ranged from 30 percent to 137 percent at spike levels of 0.05 ppm to 0.8 ppm. The median metalaxyl recovery in tomatoes is 58 percent and the mode recovery was 50 percent ± 1 percent.

In summary, method AG-395 involved blending ten grams of high moisture samples like peppers one minute in a Polytron Homogenizer with 100 mL of methanol/water (80/20, v/v). Filter through Whatman 2V filter paper then remove a two gram aliquot equivalent. Rotoevaporate to dryness then dissolve the residue in ten mL H_2O and ten mL of methanesulfonic acid. Reflux for 15 minutes. The petitioner cautions 20 minute reflux will degrade 2,6-dimethylaniline. Cool then add 15 mL hexane and 25 mL of 25 percent NaOH through the top of the condenser. Be sure the pH > 8.0. The steam distillation apparatus is a modification of the equipment proposed by Veith and Kiwus. The distillation time is approximately 1 1/4 hours. The solution is frozen. Cleanup is by silica SepPak®. The hexane is poured off the frozen water into the syringe then forced through the SepPak®. The 2,6-dimethylaniline is recovered from the SepPak® with 18 mL CH_2Cl_2. The derivative is formed by adding 200 uL of trifluoroacetic acid then rotoevaporate in a 15 °C, not 18 °C or 20 °C, water bath to just dryness. Take up in 2.0 mL toluene and transfer the toluene to a HP autosampler vial. The instrument used was a Hewlett Packard gas chromatograph, model 5880, equipped with a N/P detector and a capillary column. The columns were either a fused silica 0.25 um coating of SE-54 in a 0.2 mm x 25 m column or a wide bore 0.32 mm x 30 m fused silica column with a 0.25 um coating of DX-4. The petitioner had an adequate run table and used suitable temperature programming.

Confirmation of residues is by GC/MS using a Finnigan GC/MS, model 3200, operated in the CI mode with CH_4 as the reactant and carrier gas. The column is a glass 1.2 m x 2 mm (id) packed with 3 percent Dexsil-300 on Gas Chrom Q (80/100 mesh) operated at 100 °C. The fragment ion DMA is measured at m/e of 122 (the M + 1 ion).

The limit of detection is < 0.05 ppm. Quantitation is by the HP-1000 Lab Automation computer system. The peak heights are used for comparison of standards to unknown for software calculations. Corrections are made for recoveries and controls; and a factor 1.188 is used to convert DMA-TFA detected to metalaxyl equivalents. With n = 16 metalaxyl recoveries in peppers ranged from 74 to 126 percent at spike levels of 0.05 ppm to 1.0 ppm. Both the median and mode recovery are 84 percent.

The petitioner has presented photocopies of 45 chromatograms; 11 chromatograms for method AG-330, 22 chromatograms for method AG-348, and 12 chromatograms for method AG-395. For AG-330 all of the sample chromatograms were for tobacco extract, none showed tomato extracts. Of the 22 chromatograms presented for method 348, only four showed tomato extracts. No pepper extract chromatograms were presented for method AG-395.

RCB cannot judge the adequacy of the residue data presented until it has reviewed sufficient chromatographic supporting data. The petitioner should present photocopies of tomato extracts run by method AG-330. RCB is interested in seeing several chromatograms at or near the limit of metalaxyl detection and several chromatograms of maximum metalaxyl residues. Chromatograms should also be presented showing the results of the tomato processing study. For peppers run by method AG-395, RCB would like to see chromatograms for each variety of peppers. Also, we are interested in seeing photocopies of chromatograms of metalaxyl in peppers at or near the level of detection and several of the maximum residues detected. Photocopies of standards for the standard curves should be dated. The standards should be for the standard curves used to calculate the tomato and pepper metalaxyl results.

RCB defers judgment on the adequacy of the above methods to gather metalaxyl residue data and enforce the proposed tolerances on the fruiting vegetables group (except cucurbits) and sugar beets until we have reviewed and accepted the supporting chromatographic data we requested above.

Residue Data

Storage Stability

Storage stability studies for metalaxyl and its metabolites have been previously submitted and adequately reviewed (ibid). In summary, tobacco samples were fortified with metalaxyl at 5 ppm and frozen (to 5 °F). Sample aliquots were removed at zero days, and at one, two, four, six, and 12 months after storage commenced and analyzed for parent metalaxyl only. Tobacco metalaxyl recoveries ranged from 98 percent to 108 percent (n = 6, $\bar{X}$ = 103 % ± 4%). Potatoes spiked at the same level (5 ppm), stored under the same conditions (5 °F) with sample aliquots removed and analyzed as above had metalaxyl recoveries ranging from 71 percent to 115 percent (n = 6, $\bar{X}$ = 100% ± 16%).

Storage stability data were also presented for field incurred residues of metalaxyl on tobacco and potatoes. Tobacco was treated at three lbs (1X) and six lbs (2X) ai/acre; and potatoes were treated at 0.5 lb (1X) and one lb (2X) ai/acre. Initial residue results on tobacco from the 1X rate was 83 ppm and from the 2X rate was 128 ppm. For potatoes the initial metalaxyl results were 0.15 ppm at the 1X rate and 0.13 ppm to 0.16 ppm at the 2X rate. Eighteen months later at 5 °F, storage analysis of all samples for metalaxyl and its metabolites as the 2,6-DMA moiety gave recoveries ranging from 100 percent to 119 percent.

RCB concludes there are adequate storage stability data to support the residue data presented in this petition. Metalaxyl and its metabolites determined as 2,6-DMA are stable for at least 18 months at 5 °F.

Tomatoes

Metalaxyl and its 2,6-DMA metabolite residue data on tomatoes were presented from 15 field trials (including one processing study) for the 1979 and 1980 crop years from California(7), Florida(2), Mississippi(2), New York(3), and Ohio(1). These data have been previously submitted and reviewed (ibid). Data from these five States represent tomato production from 44,000 acres out of a national production on 128,000 acreas (see Agricultural Statistics, 1982).

Tomatoes spray treated with six to eight foliar applications of 0.375 to 0.38 lb ai/acre metalaxyl had residues of metalaxyl and its 2,6-DMA metabolites ranging from < 0.05 ppm to 0.59 ppm of which parent only residues ranged from < 0.05 ppm to 0.36 ppm at zero days PHI and at five days PHI residues ranged from < 0.05 ppm to 0.19 ppm of which parent only residues ranged from < 0.05 ppm to 0.08 ppm. At the 2X rate of 0.75 lb with six foliar applications total metalaxyl residues on tomatoes at zero day PHI ranged from < 0.06 ppm to 0.71 ppm of which parent only residues ranged from < 0.05 ppm to 0.46 ppm, and five-day PHI total metalaxyl residues ranged from < 0.05 ppm to 0.29 ppm of which parent only residues ranged from < 0.05 ppm to 0.13 ppm.

Using six foliar applications of 0.38 lb ai/acre metalaxyl in a tank mix with 1.5 lbs ai/acre chlorothalonil, total metalaxyl residues were 0.24 ppm at zero day PHI and 0.17 ppm at five days PHI.

Three of the fifteen field trials were with the proposed use. With one preplant incorporation of two lbs ai/acre and one lb ai/acre post-directed broadcast, metalaxyl residues ranged from 0.05 ppm to 0.16 ppm with PHI's from 14 to 42 days. At the 2X rate of four lbs ai/acre preplant and two lbs ai/acre postdirected broadcast metalaxyl residues ranged from 0.05 ppm to 0.36 ppm. RCB is inclined to discount the field trial with a 42-day PHI as the residue data do not reflect metalaxyl residues at the proposed uses i.e., seven days PHI.

RCB concludes the petitioner has presented sufficient geographically representative field trial residue data and that metalaxyl and its 2,6-DMA metabolite residues on tomato from the proposed uses will not exceed the requested crop group tolerance of 1 ppm.

Tomato Processing Study

The petitioner has presented the results of a tomato processing study. The study has been previously submitted and adequately reviewed (ibid). In summary, the metalaxyl residues on the RAC at the proposed use rate were 0.35 ppm (1X) and at 0.58 ppm at twice the proposed use rate. Tomatoes processed into peeled tomatoes had metalaxyl residues of 0.14 ppm (0.4X) and processed into tomato juice had metalaxyl residues of 0.21 ppm (0.60X). Thus no food additive metalaxyl tolerances are required for peeled tomatoes or tomato juice. Tomatoes processed into puree from treatment at twice the proposed use had metalaxyl residues at 1.6 ppm (2.76X). Continuing the processing to wet tomato pomace metalaxyl residues increased at 2.7 ppm (4.66X) and drying the tomato pomace showed a further increase to 9.7 ppm (16.7X). A food additive tolerance of 3.0 ppm metalaxyl on processed tomatoes has been established.

In this petition the registrant wants to raise the established dry tomato pomace tolerance from 16 ppm to 20 ppm. This proposal is consistent with RCB's policy of feed additive tolerances being based on the proposed RAC tolerance x the concentration factor and our desire to avoid "fractional" tolerances. To help prevent proliferation of tolerances, RCB suggests the petitioner submit one feed additive metalaxyl tolerance for tomato pomace in a revised Section F as follows:

Tomato Pomace (wet or dry) 20 ppm

<u>Residue Data for Tomatoes and Peppers From Metalaxyl Seed Treatment</u>

RCB has recommended favorably for a metalaxyl use and a tolerance has been established on fruiting vegetables (except cucurbits) grown from treated seeds. The data have been previously submitted and adequately reviewed (see memorandum PP#3F2827, P.V. Errico, June 15, 1983). In summary, the petitioner proposes a use of two ounces Apron® 2E (0.5 oz ai) on 100 pounds of fruiting vegetable (except cucurbit) seeds. Tomato and pepper seeds were treated with ^{14}C-phenyl metalaxyl at a rate of 0.5 oz ai (310 ppm). The seeds were planted in a field test plot and grown to maturity. The total radioactivity expressed as metalaxyl equivalents in harvested tomatoes and peppers was < 0.074 ppm in tomatoes and < 0.076 ppm in peppers.

From the approved tomato and pepper seed treatment metalaxyl uses, RCB feels it is prudent to add 0.1 ppm total metalaxyl to the tomato and pepper metalaxyl residues detected from the proposed soil applications in order to determine the proper metalaxyl tolerance for the fruiting vegetables (except curcubits) group.

<u>Peppers</u>

Metalaxyl and its 2,6-DMA metabolite residues on peppers were presented from ten field trials for the crop years 1983 and 1984 from California(2), Florida, Louisiana, Michigan, New Jersey, North Carolina(2), and Texas(2). Data from these seven States represent pepper production from 51,900 acres out of a national production on 55,500 acres (see USDA Agricultural Statistics, 1981). RCB concludes the petitioner has presented adequate geographically representative field trial data to support peppers as a representative commodity for a crop group tolerance. The petitioner presented residue data from bell peppers (5), chili peppers (2), yello wonder, tabasco, and pimento peppers. RCB concludes the petitioner has presented adequate variety data to support peppers as a representative commodity for a crop group tolerance.

With one preplant/planting incorporation of one lb ai plus two lbs ai post-directed soil applications at each at 30-day intervals metalaxyl residues on peppers at seven days PHI ranged from 0.05 ppm to 0.63 ppm, at 14 days PHI metalaxyl residues ranged from 0.05 ppm to 0.66 ppm, and at 21 days PHI metalaxyl residues ranged from 0.05 ppm to 0.37 ppm. From the 2X rate of two lbs metalaxyl at planting then two applications of one lb ai each at a 30-day interval, metalaxyl residues on peppers at seven days PHI ranged from 0.17 ppm to 0.90 ppm, at 14 days PHI metalaxyl residues ranged from 0.19 ppm to 0.98 ppm, and at 21 days PHI metalaxyl residues ranged from 0.14 ppm to 0.64 ppm.

Combining the field trial data in this petition with the seed treatment metalaxyl data, RCB concludes metalaxyl and its DMA metabolites residues on peppers from the proposed uses will not exceed the requested crop group tolerance of 1 ppm. The petitioner has presented adequate pepper variety data and sufficient geographically representative field trial data.

Since the petitioner is proposing a crop group tolerance, RCB can translate the above residue data to other fruiting vegetables (except cucurbits) such as eggplants, ground cherries, and tomatillos.

<u>Sugar Beets and Sugar Beet Tops</u>

The petitioner proposes to treat sugar beet seeds with metalaxyl. RCB has recommended favorably for a metalaxyl tolerance on garden beets and garden beet tops from a seed treatment use. The data have been previously submitted and adequately reviewed (ibid). In that review, RCB concluded the garden beet and garden beet top metalaxyl residue data from seed treatment could be translated to sugar beets and sugar beet tops for the same metalaxyl seed treatment use. RCB reiterates that conclusion.

In summary, beet seeds are treated with ^{14}C-phenyl metalaxyl at a rate of 0.5 oz ai (310 ppm). This is equivalent to treating beet seeds with Apron® 2E at a rate of two ounces (0.5 oz ai) 100 lbs of beet seeds. The beet seeds were planted in a field test plot and grown to maturity. The total radioactivity expressed as metalaxyl equivalents in beet tops at 60 days is < 0.044 ppm, and in mature beet tops is < 0.030 ppm. In the mature beets metalaxyl equivalents were < 0.031 ppm.

RCB concludes that metalaxyl and its 2,6-DMA moiety metabolite residues in sugar beets, <u>per se</u>, and sugar beet tops will not exceed the proposed 0.1 ppm tolerance from the proposed seed treatment use.

However, the petitioner has presented no data to show whether or not these residues concentrate if the sugar beets are processed into molasses, sugar, and dehydrated pulp. RCB suggests the petitioner conduct such a processing study using field incurred metalaxyl residues that result from the proposed use. After the completion of the proposed study the petitioner may need to revise his Section F with additional food and feed additive tolerances.

Residues in Meat, Milk, Poultry and Eggs

No new feeding studies were submitted with this petition. Based on the following diet, which RCB recognizes is artificial and not following standard feeding practice but one which maximizes residues fed livestock: potato meal (50% of 4 ppm), tomato pomace (25% of 20 ppm) and dry grape pomace (25% of 10 ppm) give the maximum dietary metalaxyl residues of 9.5 ppm. Though sugar beets can be major livestock feed items, only 0.1 ppm or less would be added to the above diet from the proposed use.

Livestock feeding studies have been previously submitted and adequately reviewed (op. cit.). In summary, dairy cows were fed metalaxyl at zero (control) ppm, 1.5 ppm, 7.5 ppm and 15 ppm in their feed for up to 40 days. Milk samples were collected at the end of weeks one, two, three, four then at 40 days. These milk samples were analyzed for total metalaxyl. No metalaxyl residues to the limit of detection (0.01 ppm) were detected in the milk. Cows were sacrificed three to five hours after the last feeding of metalaxyl at the end of week two, three, and four and at 40 days. Various muscle and fat samples were removed and analyzed for metalaxyl. No metalaxyl residues were detected in any of the muscle or fat samples to the limit of detection, 0.05 ppm. Liver samples at all feeding levels showed metalaxyl levels ranging from 0.11 ppm to 0.22 ppm. Kidney samples at these same metalaxyl feeding levels showed residues ranging from 0.16 ppm to 0.70 ppm. The anomalous higher residue levels in liver and kidney in the cold study when compared to the hot study are explained as being due to the short time from last feeding to slaughter. Additional feeding studies discussed previously (op. cit.) substantiate the transitory nature of metalaxyl residues in liver and kidney.

Poultry feeding studies have been previously submitted and adequately reviewed (op. cit.). No major poultry feed items are associated with the use proposed in this petition. The following poultry diet of grains (82% of 0.1 ppm), potato meal (10% of 4 ppm), dried grape pomace (5% of 10 ppm), wet tomato pomace (3% of 20 ppm) is recognized as artificial and not following standard poultry feeding practices, but a diet which maximizes residues fed to poultry. The maximum dietary burden for poultry is thus 1.62 ppm.

In summary, hens were fed a control diet, 0.05 ppm, 1.5 ppm and 5.0 ppm metalaxyl for four weeks. Eggs were collected and hens were selectively sacrificed at the end of weeks one, two, three, and four. Metalaxyl analysis of eggs, skin, fat, breast, and thigh muscle from each sacrifice showed no metalaxyl residues at the 5.0 ppm feeding level to the level of detection: < 0.1 ppm. RCB concludes the existing metalaxyl tolerances for poultry and eggs are adequate to cover the uses in this petition.

Since animal feeding studies have demonstrated the presence of low levels of metalaxyl in liver and kidney any feed use of a metalaxyl treated RAC or its byproducts must necessarily be categorized within 40 CFR 180.6(a)(1) or (a)(2). Since real residues have been found in liverstock tissues from feeding exaggerated levels of metalaxyl, RCB characterizes the proposed use as (a)(2). RCB concludes from feeding 15 ppm metalaxyl and the various feed items in our artificial diets the established secondary metalaxyl tolerance meat and meat byproducts at 0.05 ppm, fat, kidney, and liver at 0.4 ppm of cattle, goats, hogs, horses, poultry, and sheep, and eggs at 0.05 ppm, and milk at 0.02 ppm are adequate.

Other Considerations

An International Residue Limit status sheet is attached to this petition. There are no problems of compatibility with Mexican or Canadian metalaxyl tolerances for fruiting vegetables (except cucurbits) as these countries have not established metalaxyl tolerances for the fruiting vegetables (except cucurbits) group. There is a Codex tolerance for parent only metalaxyl on tomatoes at 0.5 ppm. The U.S. has objected to the exclusion of metabolites in the Codex metalaxyl tolerance expression. In a future meeting, Codex may reconsider and include the metalaxyl metabolites in the tolerance expression.

Attachment 1: International Residue Limit Status Sheet

TS-769C:RCB:Reviewer(FDG):CM#2:Rm708:557-0486:
Kenco:Job:87829:9/16/86:dej:vo:edited:fdg:
cc:R.F., Circu, TOX, EAB, EEB, FDA, PP#6F3387/6H5499,ISB/PMSD
RDI:Section Head:R.S.Quick:9/15/86

Dick Griffith 6/30/86

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Metalaxyl (Ridomil®) PETITION NO 6F3387/6H5499

CCPR NO. 138

[signature] 7/1/86

Codex Status

☐ No Codex Proposal Step 6 or above

Residue (if Step 9): parent only

Crop(s)	Limit (mg/kg)
tomatoes	0.5

Proposed U. S. Tolerances

40CFR 180.408 and
40CFR 180.561.273

Residue: metalaxyl and its metabolites*

Crop(s)	Tol. (ppm)
Fruiting Vegetables (except Cucurbits)	1.0ppm
Sugar Beets	0.1ppm
Sugar Beet Tops	0.1ppm
Dry Tomato Pomace	20.0ppm

CANADIAN LIMIT

Residue: parent only 1/

Crop	Limit (ppm)
none (on above items)	

MEXICAN TOLERANCIA

Residue:

Crop	Tolerancia (ppm)
none	

1/ On 0.1 ppm negligible residue limit for potatoes

Notes: * N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester and its metabolites containing the 2,6-dimethylaniline moiety and N-(2-hydroxy methyl-6-methylphenyl)-N-(methoxyacetyl) alanine methyl ester each expressed as metalaxyl.